A comparative study of caudal Ropivacaine versus Ropivacaine combined with Dexmedetomidine for paediatric lower abdominal surgeries

A study of 60 cases

Dissertation

Submitted in partial fulfillment of university regulations for the award of

M.D. DEGREE EXAMINATION

BRANCH X – ANAESTHESIOLOGY

THE TAMILNADU

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APRIL 2011

CERTIFICATE

This is to certify that the Dissertation ***"A Comparative Study Of Caudal Ropivacaine Versus Ropivacaine Combined With Dexmedetomidine For Paediatric Lower Abdominal Surgeries"*** presented herein by **Dr. J. BRIDGIT MERLIN** is an original work done in the Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tirunelveli for the award of Degree of M.D. (Branch X) Anesthesiology under my guidance and supervision during the academic period of 2009 - 2011.

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TIRUNELVELI MEDICAL COLLEGE AND HOSPITAL

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CERTIFICATE OF APPROVAL

This is to certify that the INSTIU TIONAL EITHICAL COMMITTEE of TIRUNELVELI MEDICAL COLLEGE AND HOSPITAL, TIRUNELVELI -11 has unanimously approved the dissertation titled Comparative study on caudal ropivacaine vs caudal ropivacaine combined with dexmedetomidine for paediatric lower abdominal surgeries" by **Dr. J.Bridgit Merlin**, MD, Anaesthesia Student, TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI -11 in its meeting held on 07.07.2010.

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DECLARATION

I, **DR. J. BRIDGIT MERLIN** declare that the dissertation titled ***"A Comparative Study of Caudal Ropivacaine versus Ropivacaine Combined with Dexmedetomidine For Paediatric Lower Abdominal Surgeries"*** has been prepared by me. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of M.D., Branch X (ANAESTHESIOLOGY) Examination to be held in APRIL 2011.

Place : Tirunelveli

Date : **DR.J.BRIDGIT MERLIN**

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CONTENTS

LIST OF ABBREVIATIONS USED

ASA	-	American Society of Anaesthesiologist
BP	-	Blood Pressure
CNS	-	Central Nervous System
CVS	-	Cardio Vascular System
EA	-	Emergence Agitation
ED	-	Emergence Delirium
FDA	-	Food and Drug Administration
FLACC	-	Faces Leg Activity Cry Consolability
GABA	-	Gamma Amino Butyric Acid
HR	-	Heart Rate
ICU	-	Intensive Care Unit
IP	-	In Patient
IV	-	Intra Venous
LMA	-	Laryngeal Mask Airway
MAC	-	Monitored Anaesthesia Care
MAP	-	Mean Arterial Pressure
mic/kg/hr	-	microgram/kilogram body weight/hour
µg/kg	-	microgram/kilogram body weight
mg/ml	-	milligram/ millilitre
ml/sec	-	millilitre/ second
NE	-	Nor Epinephrine
N_2O	-	Nitrous Oxide
O_2	-	Oxygen
PACU	-	Post Anaesthesia Care Unit
PONV	-	Post Operative Nausea and Vomiting
RS	-	Respiratory System
SD	-	Standard Deviation
SE	-	Standard Error
SpO2	-	Arterial O_2 Saturation
TIVA	-	Total Intravenous Anesthesia
Vd	-	Volume of distribution

INTRODUCTION

Pain is an unpleasant subjective sensation which can only be experienced and not expressed, especially in children. The primary reason to treat or prevent pain is humanitarian. This is even more important in children who rely completely on their parents or care givers for their well being. The concept of postoperative pain relief and its utilization in the paediatric age group has improved dramatically over the recent years.

The various methods of providing pain relief have some side effects which prohibit their use in children for eg, narcotics in children, because of their respiratory depression, the other analgesics which cannot be given for sometime after general anaesthesia due to the fear of vomiting and aspiration, the objection to the needles in the case of parenterally administered analgesics.

The regional anaesthetic techniques significantly decrease post operative pain and systemic analgesic requirements. Caudal route was chosen for this study as it is one of the simplest and safest techniques in paediatric surgery with a high success rate. Epidural space in children favours rapid longitudinal spread of drugs and makes it effective in treating postoperative pain.

Caudal block is usually placed after the induction of general anesthesia and is used as an adjunct to intraoperative anesthesia as well as postoperative analgesia in children undergoing surgical procedures below the level of the umbilicus[1]. Caudal analgesia can reduce the amount of inhaled

and IV anesthetic administration, attenuates the stress response to surgery, facilitates a rapid, smooth recovery, and provides good immediate postoperative analgesia[1]. In order to decrease intra operative and postoperative analgesic requirements after single shot caudal epidural blockade, various additives, such as morphine, fentanyl, clonidine and ketamine with local anaesthetics have been investigated[2].

Ropivacaine, a long-acting amide local anesthetic related structurally to bupivacaine, has been used for pediatric caudal anesthesia. It provides pain relief with less motor blockade. Literature suggests that ropivacaine is less cardiotoxic than bupivacaine, hence ropivacaine may be a more suitable agent for caudal epidural analgesia especially in day care surgery[3].

Dexmedetomidine is an α_2 agonist. It has an eight-fold greater affinity for α_2 adrenergic receptors than clonidine and much less α_1 effects. A major advantage of dexmedetomidine is its higher selectivity compared with clonidine for α_{2A} receptors which is responsible for the hypnotic and analgesic effects[4].

The objective of this study is to compare the analgesic effects and other effects of Dexmedetomidine when added to Ropivacaine for caudal analgesia in children undergoing lower abdominal surgeries.

AIM OF THE STUDY

1. To compare the effects of caudal Ropivacaine and Ropivacaine with Dexmedetomidine in providing post operative pain relief in children.
2. To study the other effects of caudal Dexmedetomidine
3. To establish the safety of caudal dexmedetomidine in paediatric population.

REVIEW OF LITERATURE

A.M.El-Hennawy et al[4] compared the analgesic effects and side-effects of Dexmedetomidine and clonidine added to bupivacaine in paediatric patients undergoing lower abdominal surgeries and concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly prolonged the duration of analgesia in children undergoing lower abdominal surgeries.

Mausumi neogi et al[5] did a comparative study between clonidine and dexmedetomidine used as adjuncts to ropivacaine for caudal analgesia in paediatric patients and concluded that addition of both clonidine and dexmedetomidine with ropivacaine administered caudally significantly increased the duration of analgesia.

Saadawy et al[6] studied the effect of dexmedetomidine on the characteristics of bupivacaine in caudal block in children and concluded that caudal dexmedetomidine provides excellent analgesia over a 24hr period without side effects.

G.Ivani et al[7] studied ropivacaine with clonidine combination for caudal blockade in children and concluded that the combination of clonidine 2mic/kg and ropivacaine 0.1% was associated with an improved quality of post operative analgesia compared to plain 0.2% ropivacaine without any significant post operative sedation.

Obayah et al[8] evaluated the efficacy of adding dexmedetomidine to bupivacaine on the duration of post operative analgesia in children who underwent cleft palate repair and concluded that addition of dexmedetomidine

to bupivacaine for greater palatine nerve block prolongs the post operative analgesia after cleft palate repair with clinically no relevant side effects.

Thomas R.Vetter et al[9] studied a comparison of single dose caudal clonidine, morphine or hydromorphone combined with ropivacaine in paediatric patients undergoing ureteral reimplantation and concluded that the use of caudal clonidine may be superior to caudal opiods after paediatric ureteral reimplantation.

Giovanni Cucchiaro et al[10] studied the effects of clonidine on post operative analgesia after peripheral nerve blockade in children and concluded that the addition of clonidine 1mic/kg to low concentrations of ropivacaine or bupivacaine (0.1% - 0.2%) can extend the duration of sensory block and analgesia time in children.

Akbas M et al[11] studied a comparison of the effects of clonidine and ketamine added to ropivacaine on stress hormone levels and duration of caudal analgesia and concluded that caudal 0.2% ropivacaine 0.75ml/kg with clonidine 1mic/kg for subumblical surgery attenuates changes in postoperative cortisol, insulin and blood glucose response to surgery

Sharpe et al[12] studied a comparison of caudal bupivacaine alone with bupivacaine plus two doses of clonidine for circumcision in paediatric population and concluded that there was an increase in analgesic duration with increasing doses of clonidine administered caudally and the arousal time was also prolonged.

Bock M et al[13] studied a comparison of caudal clonidine and intravenous clonidine in the prevention of agitation after sevoflurane in children and found that prophylactic use of clonidine decreases the

sevoflurane induced agitation at a dose of 4mic/kg, independent of the route of administration.

Constant I. et al[14] evaluated the addition of clonidine or fentanyl to local anaesthetics on the duration of surgical anaesthesia after single shot caudal block in children and concluded that the addition of clonidine or fentanyl to local anesthetics prolongs the duration of surgical anesthesia. Clonidine has some advantages over fenatnyl as it does not produce clinically significant side effects.

P.A.Lonnqvist et al[15] studied the pharmacokinetics after caudal block of ropivacaine (2mg/ml, 1mg/kg) in 20 children undergoing subumblical surgery and concluded that ropivacaine was well tolerated and provided satisfactory postoperative pain relief without observable motor block.

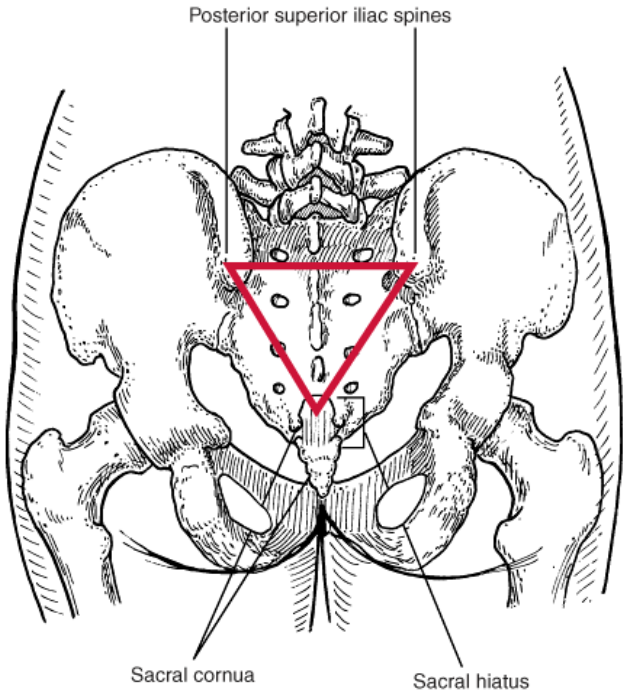
Alparslan Turan et al[16] studied caudal ropivacaine and neostigmine in paediatric surgery and found that a single caudal injection of neostigmine when added to ropivacaine offers an advantage over ropivacaine alone for postoperative pain relief in children undergoing genitourinary surgery.

ANATOMY OF CAUDAL EPIDURAL SPACE

The key to success in any regional technique is a clear understanding of the normal anatomy of the region and an appreciation of the variations that may be encountered normally. This is possible more relevant to the success of the caudal blockade than to other techniques.

Anatomy of Sacrum

Sacrum is a large triangular bone formed by the fusion of five sacral vertebrae articulating above with 5th lumbar and below with the coccyx. The base above has median and lateral positions. The median part represents the body of the 1st sacral vertebra and lateral portions, known as the alae represent fused costal and transverse elements.



The anterior surface is concave and ridged at the sites of fusion between the five sacral vertebrae. Lateral to the anterior sacral foramen through which the primary rami of the first four sacral nerves pass.

The posterior surface is convex and in the midline runs a bony ridge called the median sacral crest with three or four, but commonly four, variably prominent tubercles, representing rudimentary spinous processes.

The lamina of 5^{th} and sometimes the 4^{th} sacral vertebra fails to fuse in the midline. The deficiency thus formed is known as “SACRAL HIATUS”. The lateral margins of this each space bear a prominence. “SACRAL CORNUA” which represents the inferior articular processes of 5^{th} sacral vertebra.

Sacral Canal

It is a prismatic cavity running throughout the length of the bone and following its curves. Superiorly it is triangular in section and is continuous with lumbar epidural space.

Its lower extremity is the sacral hiatus which closed by posterior sacrococcygeal membrane which is a continuum of ligamentum flavum. Fibrous bands may be present in the canal and divide the epidural space into loculi which prevent the spread of solution and these may account for occasional incomplete anaesthesia.

Contents of Sacral Canal:

1. The dural sac extends and ends at the lower end of 2^{nd} sacral vertebra on a line joining the posterior superior iliac spine from the age of 2 years, compared to S3 – S4 at birth.
2. Sacral and coccygeal nerve roots with their dorsal root ganglia.
3. The filum terminale which is the continuation of piamater, a non nervous terminal filament of the spinal cord.
4. Epidural plexus of veins formed by the lower end of vertebral veins, a part of valveless internal vertebral venous plexus.

5. Loose areolar and fatty tissue is denser in males than in females. In infants, fat is gelatinous spongy and few connective tissues facilitates a uniform and rapid spread of local analgesic solutions. In adults it is a closed fibrous mesh texture.

It has been suggested that this difference gives rise to the predictability of caudal local anaesthetic spread in children and its unpredictability in adults.

Sacral Hiatus:

This is a triangular opening in the posterior wall of the sacrum resulting from the failure of fusion of the laminae of the 5^{th} sacral vertebra and usually part of S4. It's apex is at the level of the spine of 4^{th} sacral vertebra.

The hiatus is covered by sacrococcygeal membrane and pierced by the coccygeal nerves 5^{th} sacral nerve. The posterior sacro coccygeal membrane may be ossified in elderly subjects and making the introduction of the caudal needle almost impossible.

The distance between the sacral hiatus and dural sac may be as short as 10 mm in a neonate. In the presence of certain sacral malformations, this distance might be less and the dural sac can project even up to the level of sacral hiatus.

After the age of 6-7 years, epidural fat gets denser and is surrounded by fibrous strands, thus reducing the uniform spread of the local analgesic solutions.

The important characteristic of the caudal epidural space is that it communicates freely with the perineural spaces surrounding the spinal nerves of the lumbosacral trunk. This has several implications. Local analgesic solutions injected into the caudal space diffuse widely into the perineural

spaces, thereby improving the quality of the neural block even when dilute local analgesic solutions are used. Such a leakage into the perineural spaces also leads to an increase in the required volume of local anaesthetic. Spaces are open in children and explain why larger volumes are required in children as compared to adults.

The sacrum is cartilaginous in neonates and infants and its ossification is completed between 25 - 30 years of age. In the neonate, the long axis of the sacrum forms an acute angle with the long axis of the coccyx, thereby making it relatively easy to palpate the sacral cornua and hiatus. As the age increases, the sacrococcygeal angle also increases. Thus closing the sacral hiatus makes a caudal anaesthetic technique difficult after the age of 7 years.

When local anaesthetic solution is injected into the sacral canal, it ascends upwards in the sacral epidural space for a distance proportional to the volume of solution, force of injection, amount of leakage through the eight sacral foraminae and the consistency of the connective tissue in the space.

Favourable anatomical differences in paediatric age group against the adult are,

1) The dorsal aspect of the sacrum is almost flat in young infants and the sacral hiatus is identified by the easily palpable sacral cornua which is larger.
2) The epidural fat is very loose in infants and children. So the predictability of caudal local anesthetic spread is possible in the paediatric age group.
3) The subcutaneous tissues are also less densely packed in infants and children that make the palpation of landmark easier.

CAUDAL ANAESTHESIA

Selection of Equipment

Reliability of the technique and the incidence of complications largely depend on the characteristics of the needle used.

The four important characteristics of the needle

- Bevel
- Internal and external diameter
- Its length
- Presence of a stylet

Sharp bevelled Needle:

Advantage: Traverse easily through the tissues

Disadvantages:

1. Characteristic “give way” when sacrococcygeal membrane is punctured may not be clearly felt with sharp needles.
2. Sharp needles have long bevel advanced further into the epidural space so that it lies entirely within it.
3. Cartilaginous sacrum can be easily traversed by a sharp and long bevelled needle leading to rectal puncture or iliac vessel puncture.

Straight tipped needle with a bevel of 45 – 60 degree is ideal.

Diameter:

Small needles may bend & break during procedure. Thin needles may “give way”. Puncturing cartilaginous structures give rise to inadvertant intraosseous injection which produces effect similar to I.V. Injection. It may

enter pelvic viscera and cause damage. 21 to 23 Gauge is ideal because it is rigid and large enough to allow reflux of blood or cerebrospinal fluid.

Length:

Proximity of the dural sac makes it dangerous to use very long needles. Distance from the skin to the epidural space is almost always less than 20mm even in adults. So it is not advisable to use a needle longer than 30 mm. If needle with a stylet is used, it prevents the formation of an epidermoid tumour due to skin tag.

Epidural needle with 20 to 22 gauges are employed when one intends to use an epidural catheter via caudal route to achieve anaesthesia at higher level after radiographic conformation.

Factors determining the quality of caudal block:

- Intensity of block achieved by type and concentration of local anaesthetic.
- Height of block which depends on the volume injected

Methods for determination of the volume of Local anaesthetic:

Formula based on weight or age:

Armitage(1979) formula - Practically easy to apply

High sacral - 0.5 ml / kg

High lumbar - 1 ml/kg

Thoracic level - 1.25 ml / kg

Sclhute – Steinberg formula (up to 8-12 years)(1977)

0.1ml / segment / year

< 7 years – weight best predictor

Volume required in ml = 0.65 x number of segments to be blocked x body weight (kg)

Spiegal Formula:

Total volume of injection (ml) = 4 + (D-15) / 2 Where D is the distance seperating the sacral hiatus from the spinous process of 7^{th} cervical vertebra.

Modified spiegal formula:

Volume of injection (ml) = 4 + (D-13) / 2

Despite larger volumes of local anaesthetic used in children as compared to adults, peak plasma levels of the local anaesthetics in children remain far below the toxic levels in adults.

As the child grows, space becomes less compliant and large volume can cause higher spread of solution and thus increasing the concentration of local anaesthetics in the CSF.

Patient position:

Three positions are available for caudal anesthesia;

1. Prone position - Most often chosen in adults
2. Lateral decubitus position – This is the most commonly used position in paediatric age group.
3. Knee-chest position – This is infrequently used.

The lateral decubitus position is used in children because it is easier to maintain a patent airway in this position than in the prone position and the landmarks are more easily palpable than in adults.

Anatomical landmarks:

Classically hiatus is described as the inferior apex of an equilateral triangle formed by joining the two posterior superior iliac spines and the tip of coccyx.

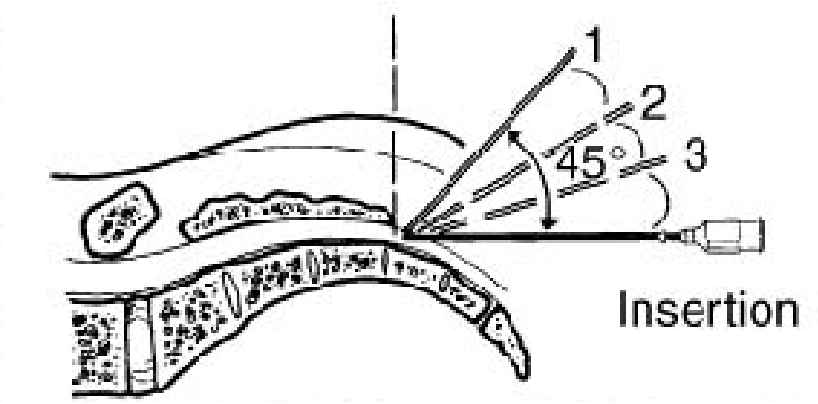
Intergluteal fold is not an ideal landmark because it will not always correspond to the midline. When the left forefinger is placed in the coccyx tip, then the hiatus corresponds to the second crease of the finger. Palpation of this membrane gives a characteristic feel of a membrane under tension similar to that of a fontanelle. The point of puncture is at the midpoint of this triangular space.

Technique:

Prepare area with an antiseptic solution

Sterile drapes are placed around the site

Puncture the skin with the needle perpendicular and bevel parallel to the long fibres of the sacrococcygeal membrane.



Once the needle crosses the sacrococcygeal membrane, a “give” is felt after which make an angle of 20-30 degree with the skin. This is done to prevent the needle hitching against the anterior aspect of the sacrum.

Advance the needle 2-3 mm, not more than the line joining the posterior superior iliac spines as to ensure that the entire bevel is within the sacral canal.

Confirmation of space:

Whoosh test:

It is done by injecting air via the needle and another person should auscultate just proximal to the injection site. If the needle is correctly positioned in the caudal space, then the characteristic whoosh sound is heard when air is pushed.

Swoosh test

If the needle is correctly positioned in the caudal space, while injecting local anaesthetics, Swoosh sound is heard at a site just proximal to hiatus,

It is useful in children to avoid air injection which cause a patchy block and a rare complication of pneumocephalus if injected in large amount of air. Venous air embolism can also occur.

Other techniques commonly used to identify the space are:

- Easy injection of drug
- No resistance to injection
- No subcutaneous bulge

Injection of Drug:

After a gentle aspiration, the drug should be injected over a period of 60-90 seconds, irrespective of the volume injected (0.023 ml – 0.033 ml / sec). Syringe should be repeatedly aspirated during the course of injection. Any change in blood pressure and heart rate should be monitored while

injection. Faster injection cause increased cephalad spread resulting in a high block and respiratory problems.

In accidental intravascular injection, fast injection will cause rapid increase in peak plasma concentration. On the other hand, too slow an injection increase the chances of lateralization of the block or a lower level of anesthesia since the drug tends to leak through the foramina or increase the risk of needle displacement.

Indications:

It is ideal for both elective and emergency lower abdominal and lower limb surgeries

Emergency : testicular torsion, strangulated hernia repair, paraphimosis, wound debridement of pelvis and lower limbs

Elective **:** Usually combined with light general anaesthesia

Repair of inguinal hernia, umbilical hernia and hydrocele

Orchidopexy, anorectal and genito urinary surgery

Pelvic, Hip and Lower extremity surgeries

Phimosis

Contraindications:

Local skin infection

Pilonidal sinus near hiatus

Major sacral malformation – Meningomyelocele

Meningitis

Spinabifida occulta – Not a contraindication

Caution:

Hydrocephalus

Convulsion disorders

Vertebral osteo synthesis

Complications:

Due to errors of needle position and puncture technique:

1. Subcutaneous injection
2. Puncturing sacral foramen – needle may enter the 3rd or 4th foramen, block of only the sacral root in question.
3. Vascular puncture – By using short bevelled needle, the incidence can be reduced.
4. Dural puncture - If dura is punctured withdraw the needle immediately, then 2nd caudal can be attempted with caution of injecting the drug under low pressure.
5. Rectal injection or intra osseous injection can occur.

Puncture complications are more common in difficult caudal.

Complications due to errors of injection:

1. **Intravascular injection;** Since epidural veins are valveless, the intra vascular injection is immediately followed by convulsions, arrythmias, hypotension and respiratory depression.
2. **Subarachnoid space injection:** It leads to total spinal anaesthesia.
3. **Hemodynamic problems:** This was rare in children below 8 years, in the absence of intravenous or subarachnoid injection.

4. **Complete or partial failure of the block:** Complete failure of block is more common after 7years of age.

Success rate increases and failure rate decreases with experience, but the failure rate will never be zero even in experienced hands.

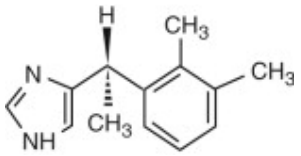
Neurologic complications:

Urinary retention is more common if are narcotics given via caudal route. The first act of micturition may be delayed but not troublesome.

Loss of consciousness is due to very rapid injection of a large volume of local anaesthetics.

Nerve lesions are rarest complication

PHARMACOLOGY OF DEXMEDETOMIDINE[17]



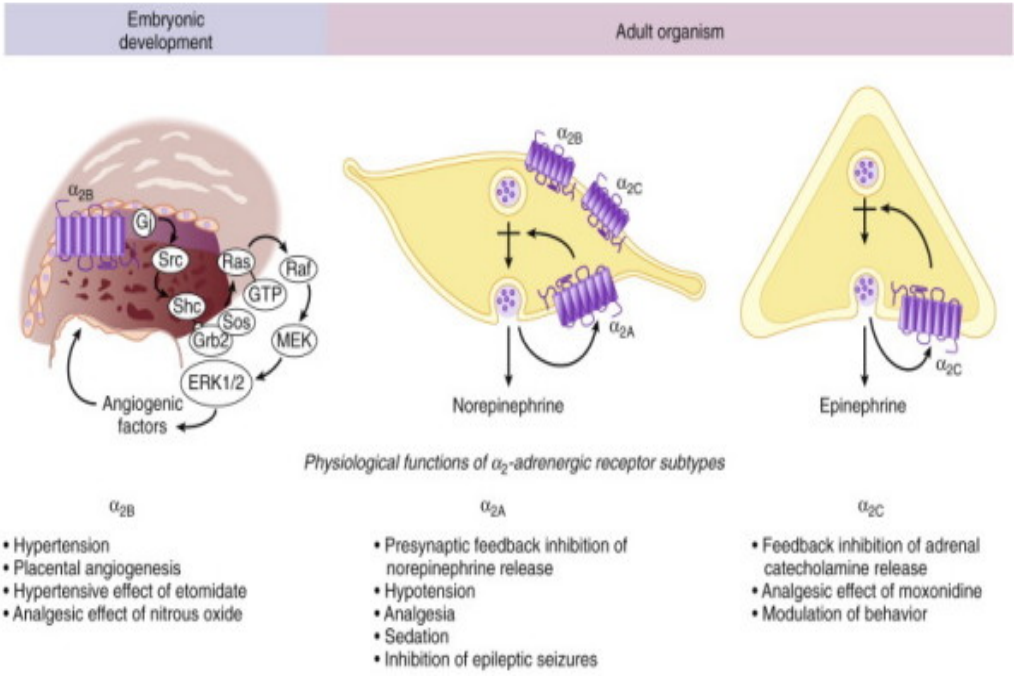
Dexmedetomidine is an α_2-agonist that received FDA approval in 1999 for use as a short-term (less than 24 h) sedative analgesic in the intensive care unit. Clonidine, the prototype of α_2-agonist, is widely used as an adjunct to anesthesia and pain medicine; however, it has been little used as a sedative.

With dexmedetomidine, there are a number of reasons for the growing and renewed interest in the use of α_2-adrenoceptors agonists as sedatives. Dexmedetomidine compared to Clonidine is a much more selective α_2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of α_1-receptors. In addition, Dexmedetomidine is a short acting drug than clonidine and has a reversal drug for its sedative effect, Atipamezole. These properties render Dexmedetomidine suitable for sedation and analgesia during the whole perioperative period: as premedication, as an anesthetic adjunct for general and regional anesthesia and as postoperative sedative and analgesic[18].

Physiology of α_2-adrenoceptors

α_2 - receptors are found in many sites throughout the body. α_2 - adrenoceptors are found in peripheral and central nervous systems, in effector organs such as the liver, kidney, pancreas, eye vascular smooth

muscles and platelets. Physiologic responses mediated by α_2 - adrenoceptors vary with location and can account for the diversity of their effects.



The different physiologic functions of α_2 adrenoreceptors. The top panel depicts the three α_2 receptor subtypes acting as presynaptic inhibitory feedback receptors to control the release of norepinephrine and epinephrine from peripheral or central adult neurons. Also, a negative feedback loop has been seen in the adrenal gland. Alpha$_{2B}$ receptors have been involved in the development of the placental vascular system during prenatal development. The lower panel lists a series of physiologic effects with its associated α_2 adrenoreceptors.(From Paris A, Tonner PH: Dexmedetomidine in anaesthesia. Curr Opin Anaesthesiol 18:412-418, 2005)

The classification of α_2 - receptors based on anatomical location is complicated since these receptors are found in presynaptic, postsynaptic and extrasynaptic locations. α_2 - adrenoceptors are divided into three subtypes; each subtype is responsible uniquely for some of the actions of α_2 - receptors.

α_{2A} - predominant subtype in CNS, is responsible for the sedative, analgesic and sympatholytic effect.

α_{2B} - found mainly in the peripheral vasculature, is responsible for the short-term hypertensive response.

α_{2C} - found in the CNS, is responsible for the anxiolytic effect[19].

All the subtypes produce cellular action by signaling through a G-protein which couples to effector mechanisms. This coupling appears to differ depending on the receptor subtype and location. The α_{2A}-adrenoceptor subtype seems to couple in an inhibitory fashion to the calcium channel in the Locus Ceruleus of the brainstem, whereas, in the vasculature, the α_{2B}-adrenoceptor sub type couple in an excitatory manner to the same effector mechanism.

Mechanism of action of Dexmedetomidine

The mechanism of action of dexmedetomidine is unique and differs from the currently used sedative drugs. α_2 - adrenoceptors are found in many sites through the CNS, however, the highest densities of α_2-receptors are found in the Locus Ceruleus, the predominant noradrenergic nuclei of the brainstem and an important modulator of vigilance. Presynaptic activation of the α_{2A} adrenoceptor in the Locus Ceruleus inhibits the release of norepinephrine (NE) and results in the sedative and hypnotic effects. In addition, the Locus Ceruleus is the site of origin for the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission. Stimulation of the α_2-adrenoceptors in this

area terminates the propagation of pain signals leading to analgesia. Postsynaptic activation of α_2-adrenoceptors in the CNS results in a decrease in the sympathetic activity leading to hypotension and bradycardia. Also, activation of the α_2-adrenoceptors in the CNS results in an augmentation of cardiac vagal activity. Combined, these effects can produce analgesia, sedation and anxiolysis.

At the spinal cord, stimulation of α_2-receptors at the substantia gelatinosa of the dorsal horn leads to inhibition of the firing of nociceptive neurons and inhibition of the release of substance P. Also, the α_2-adrenoceptors located at the nerve endings have a possible role in the analgesic mechanisms of α_2-agonists by preventing NE release. The spinal mechanism is the principal mechanism for the analgesic action of Dexmedetomidine, even though there is a clear evidence for both a supraspinal and peripheral sites of action[20].

α_2 - receptors are located on the blood vessels where they mediate vasoconstriction and on sympathetic terminals, where they inhibit NE release. The responses of activation of α_2-adrenoceptors in other areas include contraction of vascular and other smooth muscles; decreased salivation, decreased secretion, and decreased bowel motility in the gastrointestinal tract, inhibition of renin release, increased glomerular filtration, and increased secretion of sodium and water in the kidney; decreased insulin release from the pancreas, decreased intraocular pressure, decreased platelet aggregation and decreased shivering threshold by 2°C[18].

Pharmacodynamics of Dexmedetomidine

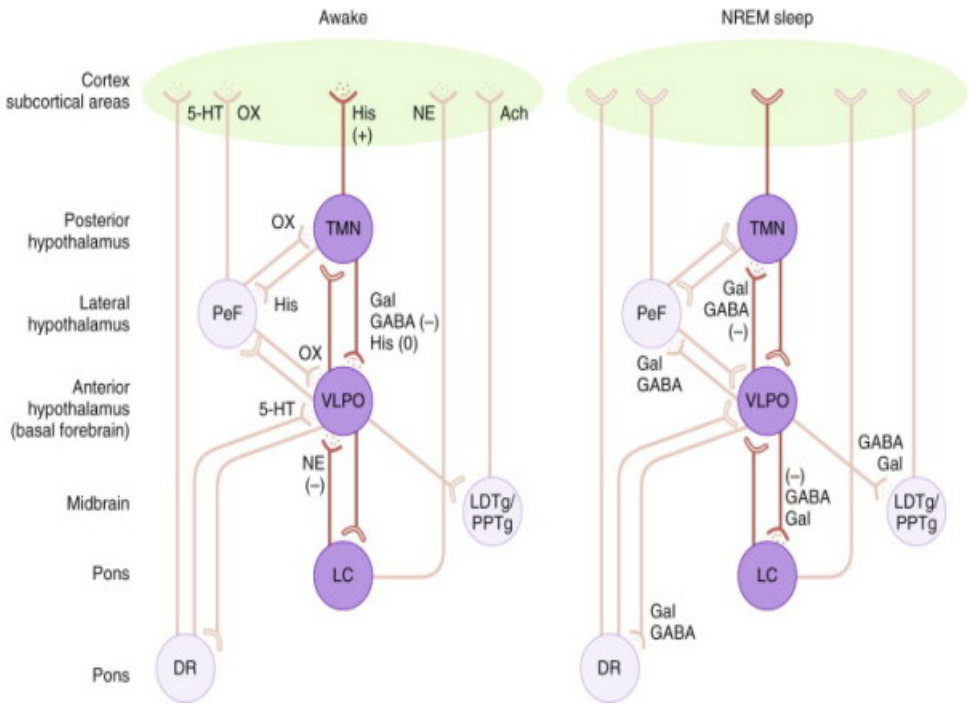
α - adrenoceptors agonists have different α_2/α_1 selectivity. Clonidine, the first developed and the most known α_2-agonist is considered as a partial α_2-agonist since its α_2/α_1 selectivity is 200:1 while the α_2/α_1 selectivity of dexmedetomidine is 1620:1 and hence it is 8 times more powerful α_2-adrenoceptor agonist than clonidine and is considered as a full α_2 adrenoceptor agonist. The α_2-adrenoceptor selectivity of dexmedetomidine is dose-dependent; at low to medium doses or at slow rates of infusion, high levels of α_2 - adrenoceptor selectivity are observed, while high doses or rapid infusions of low doses are associated with both α_1 and α_2 activities[21].

CNS effects

Dexmedetomidine induced sedation qualitatively resembles normal sleep. The participation of non rapid eye movement sleep pathways seems to explain why patients who appear to be “deeply asleep” from dexmedetomidine are relatively easily aroused in much the same way as occurs with natural sleep[22]. This type of sedation is branded “cooperative” or “arousable”, to distinguish it from the sedation induced by drugs acting on the GABA system such as midazolam or propofol, which produce a clouding of consciousness. Sedation induced by dexmedetomidine is dose-dependent; however, even low doses might be sufficient to produce sedation.

However, clinical studies showed that systemic administration of the α_2 -adrenoceptor agonists, dexmedetomidine and clonidine produce sedative and opioid-sparing effects in the perioperative setting, providing indirect evidence for some analgesic efficacy[23,24,25], although it is difficult in this special setting to distinguish between sedation and analgesia as a cause for

this opioid-sparing effect. While the analgesic effect of systemic dexmedetomidine is still debatable, administration of an α_2-agonist (clonidine) via the intrathecal or epidural route provides analgesic effects in postoperative pain and in neuropathic pain state without severe sedation. This effect is due to sparing of the supraspinal CNS sites from excessive drug exposure resulting in robust analgesia without heavy sedation.



The stimulation of the locus caeruleus (LC) by dexmedetomidine (right diagram) releases the inhibition the LC has over the ventrolateral preoptic nucleus (VLPO). The VLPO subsequently releases γ-aminobutyric acid (GABA) onto the tuberomammillary nucleus (TMN). This inhibits the release of the arousal-promoting histamine on the cortex and forebrain, inducing the loss of consciousness. (from Ebert T, Maze M: Dexmedetomidine: Another arrow for the clinican's quiver. Anesthesiology 101:569-570, 2004)

Respiratory effects

α_2 - adrenoceptors do not have an active role in the respiratory center. Therefore, dexmedetomidine throughout a broad range of plasma concentration has minimal effects on the respiratory system. Coadministration of dexmedetomidine with other sedatives, hypnotics or opioids is likely to cause additive effects.

Cardiovascular effects

Dexmedetomidine does not appear to have direct effects on the heart. In the coronary circulation, dexmedetomidine causes a dose dependent increase in coronary vascular resistance and oxygen extraction, but the supply/demand ratio is unaltered. A biphasic cardiovascular response has been described after the administration of dexmedetomidine. A bolus of 1 μg/kg results in a transient increase in blood pressure (BP) and a reflex decrease in heart rate (HR), especially in the young healthy patients. This initial response is attributed to the direct effects of α_{2B}-adrenoceptor stimulation of vascular smooth muscle. This response can be attenuated by a slow infusion over 10 min, but even at slower infusion rates, the transient increase in mean BP and the decrease in HR over the first 10 min is shown. This initial response lasts for 5 to 10 min and is followed by a decrease in BP of 10-20% below baseline and by stabilization of the HR below baseline values. Both these effects are presumably caused by an inhibition of central sympathetic outflow that overrides the direct effects of dexmedetomidine on the vasculature. Hypotension and bradycardia induced by dexmedetomidine are reversed by ephedrine and atropine respectively, but large doses are required[26]. Dexmedetomidine decreases the heart rate in dose-depemdent

mannerin children. This effect is attributed to a centrally mediated sympathetic withdrawal, which results in unregulated cholinergic activity.

Pharmacokinetics of Dexmedetomidine

Dexmedetomidine, an imidazole compound, is the active d-isomer of medetomidine. Following intravenous administration, dexmedetomidine exhibits the following pharmacokinetic parameters: a rapid distribution phase with a distribution half-life (t ½ α) of 6 min, a terminal elimination half-life (t ½ β) of 2 hours and a steady-state volume of distribution (Vss) of 118 liters and a clearance about 39L. Dexmedetomidine exhibits linear kinetics when infused in the dose range of 0.2-0.7 μg/kg/h for no more than 24 hours. Dexmedetomidine undergoes almost complete biotransformation through direct glucuronidation and cytochrome P450 metabolism. Metabolites of biotransformation are excreted in the urine (95%) and feces. It is unknown if they had intrinsic activity.

The average protein binding of dexmedetomidine is 94%, with negligible protein binding displacement by fentanyl, digoxin, theophilline,lidocaine and ketorolac. There have been no sex or age-based differences in the pharmacokinetics of dexmedetomidine. The dose of dexmedetomidine should be decreased in patients with hepatic or renal impairment. Dexmedetomidine does cross the placenta and should be only used during pregnancy if the potential benefits justify the potential risk to fetus.

Dexmedetomidine is a white powder that is freely soluble in water and has a pka of 7.1. It is supplied as 100 µg/ml 2 ml vial which must be diluted with 48 ml of 0.9% sodium chloride prior to administration. For adult patient, dexmedetomidine is administered by a loading infusion of 0.5-1 µg/kg over 10 minutes, followed by a maintenance infusion of 0.2 to 0.7 µg/kg/h. The effect appears in 5-10 min, and is reduced in 30-60 min. The maintenance infusion is adjusted to achieve the desired level of sedation.

The most frequently observed adverse events in patients receiving dexmedetomidine for ICU sedation include hypotension, hypertension, nausea, bradycardia and atrial fibrillation. Most of these events occur during or after the loading dose, therefore, reducing or omitting the loading dose could result in decreasing the incidence and severity of these adverse events.

Appropriate patient selection for dexmedetomidine administration is crucial; because it decreases sympathetic nervous activity, its effects may be most pronounced in patients with decreased autonomic nervous system control such as the elderly, diabetic patients, patients with chronic hypertension or severe cardiac disease such as valve stenosis or regurgitation, advanced heart block, severe coronary artery disease or in patients who are already hypotensive and/or hypovolemic.

Dexmedetomidine does not affect the synthesis, storage or metabolism of neurotransmitters and do not block the receptors, thus providing the possibility of reversing the hemodynamic effects with vasoactive drugs or the specific alpha2-antagonist, Atipamezole which acts by increasing the central turnover of norepinephrine. Its duration of action is 2 hours[27].

Perioperative uses of dexmedetomidine

I – Premedication

Dexmedetomidine possesses anxiolytic, sedative, analgesic, antisialogogue and sympatholytic properties, which render it suitable as a premedication agent. Dexmedetomidine potentiates the anesthetic effects of all intraoperative anesthetics (intravenous, volatile or regional block). Bohrer[28] showed that preoperative administration of intravenous or intramuscular dexmedetomidine resulted in a decrease in the induction dose of thiopentone by up to 30%. The administration of intramuscular dexmedetomidine at a dose of 1 μg/kg for premedication in outpatient cataract surgery resulted in sedation, and decrease in intraocular pressure without significant hypotension or bradycardia[29,30.] Also the administration of dexmedetomidine for premedication decreases oxygen consumption intraoperatively by 8% and postoperatively by 17%. Indications for the use of dexmedetomidine as premedication include patients susceptible to preoperative and perioperative stress, drug addicts and alcoholics, chronic opioid users and hyertensive patients.

II – Intraoperative uses of dexmedetomidine

Intraoperative uses of dexmedetomidine include its use as an adjunct to general anesthesia, as an adjunct to regional anesthesia, in monitored anesthesia care (MAC) or as a sole agent for total intravenous anesthesia (TIVA).

1– Use of dexmedetomidine as adjunct to general anesthesia

The use intraoperative dexmedetomidine may increase hemodynamic stability because of attenuation of the stress-induced sympathoadrenal responses to intubation, during surgery and during emergence from anesthesia. Talke[31] evaluated the effects of varying plasma concentrations of dexmedetomidine on HR, BP and catecholamines concentrations during emergence from anesthesia in the setting of vascular surgery. This study demonstrated that dexmedetomidine attenuates the increases in heart rate and plasma norepinephrine levels observed during the emergence from anesthesia.

Administration of intravenous dexmedetomidine produces an anesthetic-sparing effect. Aho[32] showed 25% reduction of maintenance concentrations of isoflurane in patients undergoing hysterectomy. Khan found 35%-50% reduction in isoflurane concentrations with either low or high doses of dexmedetomidine. Fragen[33] noted 17% reduction in sevoflurane requirements for maintenance of anesthesia in elderly patients. In addition, the use of dexmedetomidine produces intraoperative and postoperative opioid-sparing effect. Aho[24] administered dexmedetomidine at dose of 0.4 μg/kg in patients undergoing laparoscopic tubal ligation and found a 33% decrease in morphine use postoperatively.

Talke[34] investigated the muscle relaxant effects of dexmedetomidine on the neuromuscular junction and found no clinically relevant effects. Dexmedetomidine reduces the vasoconstriction threshold and the shivering threshold and is associated with a lower incidence of shivering[18].

2 – Use of dexmedetomidine for regional anesthesia

The use of dexmedetomidine as adjuvant in regional anesthesia is still not validated. Maarouf[35] explored the effect of epidural dexmedetomidine on the incidence of postoperative shivering in patients undergoing orthopedic surgery. He found that patients who received dexmedetomidine at a dose of 100 µg added to 20 ml 0.5% bupivacaine showed lower incidence in postoperative shivering when compared to patients who received epidural bupivacaine alone (10% vs.36%). Memis[36] noted that the addition of 0.5 µg/kg dexmedetomidine to lidocaine for intravenous regional anesthesia improves the quality of anesthesia and perioperative analgesia without causing side effects. Kanazi et al[37]investigated the effect of adding a small dose of 3 µg of intrathecal dexmedetomidine to 12 mg bupivacaine. They found a significant prolongation of sensory and motor block as compared to bupivacaine alone. In this study, the effect of 3 µg intrathecal dexmedetomidine was similar to that produced by the addition of 30 µg of intrathecal clonidine.

3 – Use of dexmedetomidine in monitored anesthesia care

Dexmedetomidine confers arousable sedation with ease of orientation, anxiolysis, mild analgesia, lack of respiratory depression and hemodynamic stability at moderate doses. These properties allow dexmedetomidine to be an almost ideal agent for MAC despite its lack of amnesia and poor controllability because of its slow onset and offset. The efficacy, side effects, and recovery characteristics of dexmedetomidine were compared to propofol when used for MAC[25]. This study showed that dexmedetomidine achieved similar levels of sedation to propofol, albeit with a slower onset and offset of sedation. Neither dexmedetomidine nor propofol influenced respiratory rate, but propofol

resulted in lower mean arterial pressure during the intraoperative period. In the recovery room, dexmedetomidine was associated with an analgesia-sparing effect, slightly increased sedation, but no compromise of respiratory function or psychomotor responses. Dexmedetomidine in MAC was used successfully in many situations: when patient arousability needed to be preserved, as for awake craniotomy, for awake carotid endarterectomy and for vitreoretinal surgey. In addition, dexmedetomidine was used for sedation in difficult airway patients; during fiberoptic intubation, and for sedation of a patient with difficult airway undergoing lumbar laminectomy surgery in the prone chest position under spinal anesthesia.

4 – Use of dexmedetomidine as a sole anesthetic agent

Ramsay[38] has used dexmedetomidine as a sole anesthetic agent. The report describes three patients who presented for surgery with potential airway management challenges. Dexmedetomidine was infused in increasing doses (up to 10 µg/kg/h) until general anesthesia was attained. No respiratory depression was noted, only one patient required chin lift. Also no hypotension or severe bradycardia were noted. The rationale for this use of dexmedetomidine is based on its known properties to provide sedation, analgesia while avoiding respiratory depression at low doses. These effects were maintained at higher doses without hemodynamic instability.

III – Use of dexmedetomidine in the postoperative period

Dexmedetomidine special properties favour its use in recovery room. In addition to its sympatholytic effects, analgesic effects and decreased rate of shivering, the preservation of respiratory function allows the continuation of the dexmedetomidine infusion in the extubated, spontaneously breathing

patient. The possibility of ongoing sedation and sympathetic block could be beneficial in reducing high rates of early postoperative ischemic events in high-risk patients undergoing non-cardiac surgery. During emergence from anesthesia, dexmedetomidine reduces NE levels significantly. However, patients who received intraoperative dexmedetomidine needed more fluids to avoid hypotension, a side effect that may be unfavorable in volume-sensitive patients with reduced left ventricular function. In addition, care should be taken in patients who depend on a high level of sympathetic tone or in patients with reduced myocardial function who cannot tolerate the decrease in sympathetic tone[18]. Perioperative administration of dexmedetomidine could be beneficial in chronic opioid users and alcoholics, in high-risk patients as well as in cardiac patients with good to moderately decreased left ventricular function.

IV – Use of Dexmedetomidine in the pediatric-age group

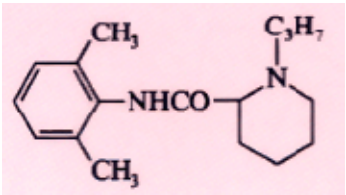
Only few case reports about the use of dexmedetomidine in the pediatric age group are found in the literature[39, 40]. Tobias[39] used dexmedetomidine for ICU sedation in a10-week old infant requiring mechanical ventilation and in a 14-y old patient after posterior spinal fusion for scoliosis. The use of dexmedetomidine at a dose of 0.25 µg/kg/hr for 24 h in these two cases resulted in acceptable sedation without significant hemodynamic changes. Dexmedetomidine was also used for sedation and anesthesia in an 11-y old patient undergoing gastroscopy; however, it resulted in insufficient sedation. Another study conducted in pediatric-age group explored the use of intraoperative dexmedetomidine at different doses with the goal of reducing the post sevoflurane agitation in children aged 1-10 y.

The optimal dose of dexmedetomidine was 0.3 μg/kg and its use did not result in adverse effects[41]. When compared with propofol for sedation during MRI, dexmedetomidine provides adequate sedation during the scan but has a slower recovery profile[40].One of the major advantages of dexmedetomidine over other sedatives is its respiratory effects, which are minimal in adults and children. it does not lead to extreme hypoxia or hypercapnia. Indeed, respiratory rate, CO_2 tension, and oxygen saturation are generally maintained during dexmedetomidine sedation in children.[40]

PHARMACOLOGY OF ROPIVACAINE

Ropivacaine, a new long acting amide local anesthetic was introduced in 1992. It has a propyl group but bupivacaine has a butyl group on the piperidine nitrogen atom of the molecule which was first synthesised in 1957[42]. Though it has similar structure, pharmacology and pharmacokinetics to that of bupivacaine, Ropivacaine has lower potential for toxic effect. Ropivacaine is a pure (s – isomer) enantiomer. On mg basis ropivacaine shows greater selectivity for sensory blockade and a lower systemic toxicity as compared to bupivacaine.

Chemical name: **(**S) – 1 propyl 2',6' pipecoloxylidide hydrochloride monohydrate



Formula : $C_{17}H_{26}N_2O$

Physicochemical properties:

Molecular mass	:	274.4gm/mol
pKa	:	8.1
Solubility in water at 25^0C	:	53.8g/L
Protein binding	:	94%
Volume of distribution	:	41 L

Mechanism of action

Ropivacaine reversibly interferes with the entry of sodium ion to the nerve cell membranes, leading to decreased membrane permeability to sodium and raises the threshold for electrical excitability. The order of blockade affecting the nerve fibres is: autonomic, sensory and motor; and the effect disappears in the reverse order. Clinically the order of loss of sensations is: pain, temperature, touch, motor and proprioception.

Pharmacokinetics

It has bioavailability of about 87%- 98% when administered epidurally. The absorption depends on the total dose, route, concentration of the drug and the patients's haemodynamic condition and the vascularity of the administration site. The onset of action begins at 10 – 25 min after epidural administration, 5min after spinal administration, 15-30 min after major nerve block and 1- 15 min after field block.

Ropivacaine is extensively bound to plasma proteins (94 %), mainly α 1 acid glycoprotein and the systemic toxicity is related to unbound drug concentration. It crosses the placenta. It is metabolised by Cytochrome P450 1A by aromatic hydroxylation to 3'OH Ropivacaine and 4'OH Ropivacaine. It has a halflife of about 1.6 – 6hrs which varies with the route of administration. 86% of the drug is eliminated in urine. It has greater clearance and shorter elimination half life as compared to bupivacaine. It also has decreased lipid solubility and decreased Vd as compared to bupivacaine.

Uses

Ropivacaine is indicated for local anaesthesia including infiltration, nerve block, epidural and intrathecal anaesthesia in adults and childrens. It is also indicated for peripheral nerve block and caudal epidural in children for surgical pain. It is also sometimes used for infiltration anaesthesia for surgical pain in children.

Adverse effects

Mostly they are related to administration technique, resulting in systemic exposure or pharmacological effects of anaesthesia. Allergic reactions can also occur. Systemic exposure to excessive quantities of ropivacaine mainly results in CNS and CVS effects. CNS effects usually occur at lower plasma concentration.

CNS effects

It may include CNS excitation (nervousness, tingling around the mouth, tinnitus, tremor, dizziness, blurred vision, seizures) followed by depression (drowsiness, loss of consciousness, respiratory depression and apnea).

CVS effects

It includes hypotension, bradycardia, arrhythmias, and/or cardiac arrest. Some of which may be due to hypoxemia secondary to respiratory depression

As for bupivacaine, there is evidence that Intralipid a commonly available intravenous lipid emulsion can be effective in treating severe cardiotoxicity

EMERGENCE DELIRIUM IN CHILDREN[43]

Emergence delirium (ED) is not a new phenomenon in clinical practice. In the early 1960s, Eckenhoff et al[44] were the first to report the signs of hyperexcitation in patients emerging from ether, cyclopropane, or ketamine anesthesia, particularly when administered for tonsillectomy, thyroidectomy, and circumcision. Children experienced postanesthesia agitation more often than adults (12%–13% vs 5.3%) [45]. With the recognition of postoperative pain management in children and the increased use of analgesics, the incidence of emergence agitation (EA) was attenuated. However, with the introduction into clinical practice of the new short-acting, volatile anesthetics sevoflurane and desflurane, the problem of ED reemerged[46]. When children were aroused from anesthesia in a quiet manner, they suddenly entered, often due to an external stimulus, a state of excitation in which they could not be consoled by the usual methods[47]. Restless recovery from anesthesia may not only cause injury to the child or to the surgical site, but may also lead to the accidental removal of surgical dressings, IV catheters, and drains. Extra nursing care may often be necessary as well as supplemental sedative and/or analgesic medications, which may delay patient discharge from hospital. This adverse postanesthesia event raises the question about the “quality” of a particular anesthetic. Parents who witness ED in their child may worry about permanent sequelae.

Sikich and Lerman[48] defined ED as “a disturbance in a child’s awareness of and attention to his/her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive

motor behaviour in the immediate postanesthesia period." ED usually occurs within the first 30 min of recovery from anesthesia, is self-limited (5–15 min), and often resolves spontaneously.

The incidence of EA/ED largely depends on definition, age, anesthetic technique, surgical procedure, and application of adjunct medication. Generally, it ranges from 10% to 50%[44,49,50], but may be as high as 80%[51] .

ANESTHESIA-RELATED FACTORS

Rapid Emergence

Postanesthesia agitation has been noted more often with the newer, less soluble, inhaled anesthetics, such as desflurane and sevoflurane, than with other volatile ones. It has been postulated that rapid awakening after the use of the insoluble anesthetics may initiate EA/ED by worsening a child's underlying sense of apprehension when finding himself in an unfamiliar environment. Some parents claim the patient's behaviour upon emergence was the same as when he was suddenly awakened from deep sleep[47]. Older children and adults usually become oriented rapidly, whereas preschool-aged children, who are less able to cope with environmental stresses, tend to become agitated and delirious. However, recovery from propofol anesthesia is also rapid, smooth and pleasant. Several studies have shown that sevoflurane anesthesia is associated with a higher incidence of EA/ED compared with propofol[52-55]. Delaying emergence by a slow, stepwise decrease in the concentration of inspired sevoflurane at the end of surgery did not reduce the incidence of EA.

Intrinsic Characteristics of an Anesthetic

Most authors have documented that EA/ED occurs more often after sevoflurane than after halothane anesthesia[49]. Some authors have speculated that two unique, intrinsic characteristics of sevoflurane might account for the development of EA/ED[46]. First, this anesthetic exerts an irritating side effect on the central nervous system (CNS). Second, although sevoflurane degradation products appear to cause no organ damage themselves, data are lacking on their possible interactions with other types of medications. As for the eventual neurotoxic influence of sevoflurane degradation products, there is no supporting scientific evidence.

SURGERY-RELATED FACTORS

Pain

Postoperative pain has been the most confounding variable when assessing a child's behavior upon emergence because of the overlapping clinical picture with EA/ED. Inadequate pain relief may be the cause of agitation, particularly after short surgical procedures for which peak effects of analgesics may be delayed until the child is completely awake. In several studies, the preemptive analgesic approach successfully reduced EA/ED, suggesting that pain may be its major source[56]. Bock et al[13] studied the effect of clonidine on EA in 80 children aged 3–8 yr undergoing minor day-case surgery who were anesthetized with sevoflurane. The children received a caudal block for perioperative pain relief. A dose of 3μ/kg clonidine was found to prevent agitation whether administered IV or caudally. Other authors demonstrated that an IV dose of 2μ/kg clonidine was efficient under similar conditions[51,57]. Another more selective α_2 receptor agonist, dexmedetomidine,

also reduced sevoflurane-induced EA/ED when given prophylactically[41,58]. On the other hand, post anesthesia agitation has been observed when pain was efficiently treated[49,50,59]or even when absent[53]. Weldon et al[59] studied 80 premedicated children aged 12 months to 6 years undergoing inguinal hernia repair, whose postoperative pain was managed with a preemptive caudal block. At 5 min after arrival in the PACU, agitation was significantly more frequent in sevoflurane anesthetized children compared with halothane anesthetized children (26% vs 6%). A higher incidence of EA was also recorded in patients who received sevoflurane for non painful interventions, such as magnetic resonance imaging scanning and eye examinations[53]. In contrast, children anesthetized with halothane and propofol for the same procedures, respectively, were free of agitation. These findings clearly suggest that EA/ED may be a clinical phenomenon that is separate from pain.

Surgery Type

Surgical procedures that involve the tonsils, thyroid, middle ear, and eye have been reported to have higher incidences of postoperative agitation and restlessness. Eckenhoff et al[44] speculated that a “sense of suffocation” during emergence from anesthesia may contribute to EA in patients undergoing head and neck surgery. However, there are no supporting scientific data to date.

PATIENT-RELATED FACTORS

Age

Aono et al[49] found that ED appeared more often with sevoflurane than with halothane in preschool boys aged 3–5 yr (40% vs 10%). The difference was not observed in the school-aged population. All children received oral diazepam for premedication and a caudal block for peri operative pain control. The authors speculated that the psychological immaturity of preschool children, coupled with the rapid awakening in a strange environment, may have been the main cause of ED. Generally, younger children are more likely to show altered behaviour upon recovery from anesthesia. The subpopulation of those aged 2–5 yr seems to be the most vulnerable as they are easily confused and frightened by unexpected and unpredictable experiences. In a recent commentary on the diagnosis of delirium in pediatric patients, Martini[60] addressed the role of brain maturation in the genesis of this phenomenon. He pointed out that the pediatric brain is almost a mirror image of a normal age-related regressive process with a consequent decline in norepinephrine, acetylcholine, dopamine and γ amino butyric acid (GABA). Thus, the development of cholinergic function and the hippocampus may suggest clues about the relative susceptibility of younger children to delirium.

Preoperative Anxiety

Intense preoperative anxiety, both in children and their parents has been associated with an increased likelihood of restless recovery from anesthesia.

Temperament

Children who are more emotional, more impulsive, less social and less adaptable to environmental changes were identified to be at risk for developing postanesthesia agitation. It is likely that there is some substrate innate to each child that will elicit, to a larger or lesser extent, a fearful response to outside stimuli, depending on the interaction between the child and the environment. This reactivity, which describes the “excitability, responsivity or arousability” of the child, might be the underlying substrate from which both preoperative anxiety and ED arise. Patient-related factors are an important source of variability among studies in the incidence of EA/ED as they are most difficult to control when investigating this phenomenon.

ADJUNCT MEDICATION

Numerous drugs, including anticholinergics, droperidol, barbiturates, opioids, benzodiazepines, and metoclopramide, may contribute to behavioural disturbances after anaesthesia.

In summary, none of the above-discussed factors had been proven to be the sole underlying cause of EA/ED. However, each factor, especially when combined with the others, may influence the behaviour of a child emerging from anaesthesia.

PREVENTION AND TREATMENT

Given that the EA/ED etiology is still unknown, a clear-cut strategy for its prevention has not been developed. Data on the possible role of premedication in reducing EA/ED have been conflicting. Sevoflurane at high concentrations has been shown to enhance and at low concentrations to block the GABA -A receptor-mediated inhibition of neurotransmission in the CNS. On the other hand, there are studies in which midazolam premedication did not show any benefit on the quality of recovery from anesthesia . This finding may possibly be the result of applying a nonspecific measuring tool or a provision of inadequate pain control. Benzodiazepines themselves are associated with paradoxical reactions and agitation that are reversed with flumazenil[61]. Furthermore, the antianalgesic effects of midazolam might worsen pain and increase the incidence of nonspecific agitation that resembles ED.

Various preemptive analgesic approaches, including caudal block[59], fentanyl, ketorolac, clonidine[13,57] and dexmedetomidine[41,58], have been recommended to eliminate pain as a potential source of discomfort and agitation. The decision of whether to treat EA/ED with additional medication depends upon the severity and duration of symptoms. Many studies have shown that EA/ED is self-limited, resolving without pharmacological Intervention over time[16]. “Rescue” medication includes analgesics, benzodiazepines, and hypnotics. A single bolus dose of dexmedetomidine 0.5μ/kg was also shown to be efficient in the PACU for ED[62].

PAIN ASSESSMENT IN CHILDREN

“Pain is a unique, highly subjective multidimensional experience encompassing many sensory & affective components". Pain assessment is the most important and critical component of pain management. Assessment and management are interrelated. If pain can be assessed accurately, adequate and appropriate management can be implemented.

Assessing pain in children is an ever challenging as well as a difficult task, mainly because so far no reliable method of assessing and measuring child’s pain is available. Various methods available are,

1. Physiological measures
2. Self reporting measures
3. Behavioral measures

Physiological measures

Changes in pulse, blood pressure and respiration reflect autonomic arousal. Autonomic responses to pain and their measurement form an important aspect of certain pain scales. Metabolic changes cause release of catecholamine, growth hormone, glucagon, cortisol, aldosterone and beta endorphins which have been documented in infants and children following noxious stimulation. Only plasma cortisol have been shown to correlate with behavioral responses to noxious stimuli.

Self reporting measures

1. VISUAL ANALOGUE SCALE: Visual analogue scale is the accepted and popular method of measurement of pain in adults and provides reproducible results in children down to an age of five years. VAS using 10 cm length scale marked “no pain” at one end to “excruciating pain” at the other end with 1 mm or 1 cm segments. The child is asked to identify a point on the scale which corresponds to his pain. A score of less than 4 is no pain, less than 6 implies tolerable pain and more than 6 means he needs medication. VAS can also be a 50 cm long, linear scale with no pain at one end and excruciating pain at the other end with no intermediate division but with descriptive red white colorings.
2. OUCHER’S SCALE: This scale displays six photographs of a child’s face showing increasing levels of discomfort. This scale is based on the mimic, vocalization and irritability. Features characteristic of increasing pain are;
    a. Distortion of face such as lowering of the brow, broadening of the nasal root, angular and squarish mouth, tightly closed eyes and tightening of the jaw.
    b. Vocalization, changing from sobbing to pain cry.

    The children are asked to show the face which mimicked their expression
3. THE POKER CHIP SCALE: It quantitates the child's pain by the number of chips (0–4), he/she selects "pieces of hurt".
4. Analogue Chromatic Continuous Scale (ACCS): This system is potentially is useful for children as young as 3 years old. Children tend to associate red and black colors with increased pain sensation. (The back is ruled for easy scoring).

Behavioural Observation Methods

Behavioural observation methods are the primary approach to accessing pain information from preverbal and nonverbal children. Unfortunately, development of these methods lags behind self-report approaches. They score the behaviours which represent the reaction to pain and the scores are allotted according to the degree of alteration of a particular behaviour. The behaviours scored include vocal behaviours such as cry, scream, verbally expressed pain and anxiety and non verbal behaviours such as muscle rigidity, torso movements, leg movements and facial expression.

The PBRS, CHEOPS[2, 14], CHIPPS[41] and TPPPS[16]: Pain Behavior Rating Scale, Children's Hospital Eastern Ontario Pain Scale, Children and Infants Postoperative Pain Scale and Toddler- Preschooler Postoperative Pain Scale are such scales. The observation in these scales has an observer bias. The OBJECTIVE PAIN SCALE[3] measures pain as a physiological variable-blood pressure along with behavioral changes. This has been shown to be a sensitive and reliable tool in evaluating postoperative pain in children who are not able to verbally comment upon their pain. This takes into account the systolic blood pressure, cry and its response, movement, agitation and verbal evaluation as described by Hannallah RS.

FLACC[4, 9, 63] and CHEOPS[2] are for acute procedural and postoperative pain; the COMFORT scale for children in intensive care and the Parents Postoperative Pain Measure (PPPM) for postoperative pain managed by parents at home[64].

MATERIALS AND METHODS

Study design:

Prospective randomized comparative observer blinded study.

Population:

60 patients

Inclusion criteria:

ASA I and II patients between 6 months to 6 years of age undergoing lower abdominal surgeries.

Sample size;

- Group RD (n = 30) – Caudal 0.25% Ropivacaine 1ml/kg with Dexmedetomidine 2mic/kg making the volume to 0.5ml
- Group R (n = 30) – Caudal 0.25% Ropivacaine 1ml/kg + 0.5ml normal saline

Exclusion criteria :

1. Suspected coagulopathy
2. Infection at the site of caudal block
3. History of developmental delay
4. Neurological diseases
5. Skeletal deformities
6. Allergy to local anaesthetics

Pre operative evaluation:

In all children, age, I.P. No., body weight, and baseline vital parameters were recorded. History regarding previous anaesthesia, surgery, any significant medical illness, medications and allergy were recorded. Complete

physical examination and airway assessment were done. Following laboratory investigations were done: haemoglobin %, blood sugar, urea, serum creatinine and urine analysis.

Study Method:

After getting institutional ethical committee approval and written informed consent from parents, the patients were randomly allocated into two groups. Group R (n = 30) was taken as Ropivacaine group and Group RD (n=30) as Dexmedetomidine group.

All the patients were premedicated with Inj.Atropine 0.02mg/kg i.m. 45 min prior to anaesthesia. Induction of anaesthesia was achieved with 50% N_20 and 8% sevoflurane in oxygen in spontaneous ventilation. Appropriate size LMA was inserted. After the insertion of LMA, Sevoflurane concentration was reduced to 3% in 50% nitrous oxide, patients were left in spontaneous ventilation and a caudal block was performed in all patients according to the group. The inhaled concentration of sevoflurane was adjusted to achieve haemodynamic changes < 30% of the baseline values[4]. No other narcotics, analgesics or sedatives were used intra operatively.

Standard monitoring was used during anaesthesia and surgery. HR, MAP and SpO_2 were recorded before surgery and every 5min till the end of surgery.

The occurrence of intraoperative hypotension requiring a fluid bolus, bradycardia requiring atropine and the maximum maintenance concentration of sevoflurane(%) were recorded.

Behaviour during emergence was rated on a four-point scale[41, 49]:

1. Calm
2. Not calm but could be easily calmed
3. Not easily calmed, moderately agitated or restless
4. Combative, excited, or disoriented.

Using the paediatric observational FLACC pain scale with its 0 – 10 score range, each patient's pain intensity was assessed at the end of surgery and then every 4 hr for 24 hr after operation. If the FLACC pain scale was 4 or more, syrup paracetamol 15mg/kg was administered. The duration of analgesia (from the time of caudal injection to the time at which FLACC score 4 or more) was also recorded. Sedation score was assessed using Ramsays sedation scale as follows.

1. Anxious and agitated or restless, or both
2. Co-operative, oriented, and calm
3. Responsive to commands only
4. Exhibiting brisk response to light glabellar tap or loud auditory stimulus
5. Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus
6. Unresponsive

The following times were recorded:

1. The anaesthesia time (time from induction of anesthesia to the end of surgery when sevoflurane discontinued).
2. Time from caudal block to skin incision.
3. Time from caudal block to end of surgery.

4. Emergence time (time from the end of surgery to opening the eyes on calling).

Complications such as PONV, respiratory depression, hypotension and bradycardia were also noted. Respiratory depression was defined as a decrease in SpO2 of <95% requiring supplementary oxygen. Hypotension was defined as systolic arterial pressure 70 plus twice the age in years and associated with altered peripheral perfusion. Bradycardia was defined as heart rate below 80 beats/ min for ages, 1 yr and 60 beats/ min for ages above 1 yr. Delayed anaesthetic emergence was defined as 20 min elapsing from the end of surgery to exiting the operating theatre[4].

Failure of caudal block was defined as any increase in HR or MAP >20% than pre incision values[4].

STATISTICAL ANALYSIS

Data were analysed using SPSS version 13.0 computer software. Numerical variables were presented as mean and standard deviation (SD) and categorical variables were presented as frequency (%). Student 't' test was used for between-group comparisons between categorical variables. Time to first analgesic administration was analysed by the Kaplan–Meier survival analysis[4].

RESULTS

In this study, I encountered 8 failed caudal blocks. Those cases were eliminated from the study. Age, weight of the children and duration of surgery between both the groups were comparable and were not statistically significant (P>0.05).

Table 1. Comparison of age group between both groups

Age in months	RD group		R group		Total	
	No	%	No	%	No	%
6 – 12	5	16.7	4	13.3	9	15.0
13 – 24	7	23.3	3	10.0	10	16.7
25 – 36	5	16.7	3	10.0	8	13.3
37 – 48	4	13.3	4	13.3	8	13.3
49 – 60	2	6.7	8	26.7	10	16.7
61 – 72	7	23.3	8	26.7	15	25.0
Total	30	100.0	30	100.0	60	100.0
Mean ±SD	40.7 ± 22.1		48.9 ± 21.5		44.8 ± 22.0	
Significance	P > 0.05					

The mean age of the RD group was 40.7 ± 22.1 months and the R group was 48.9 ± 21.5 months. The difference between the two groups was not statistically significant (P > 0.05).

Figure.1.Comparison of age group between both groups

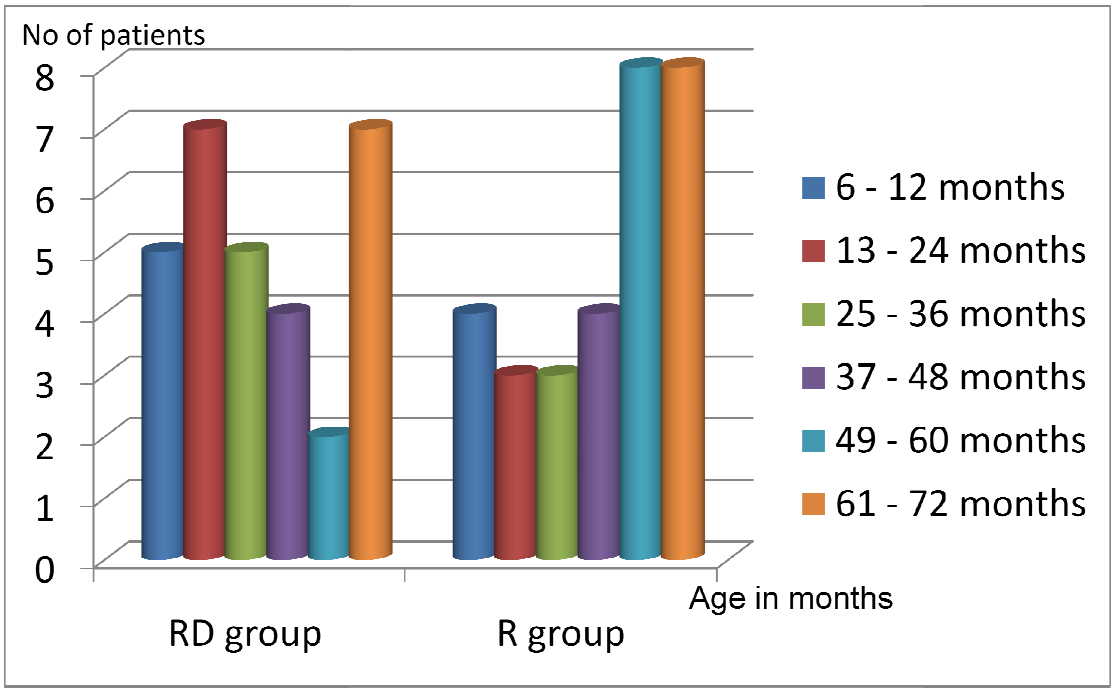


Table. 2. Distribution of sex in between RD and R groups

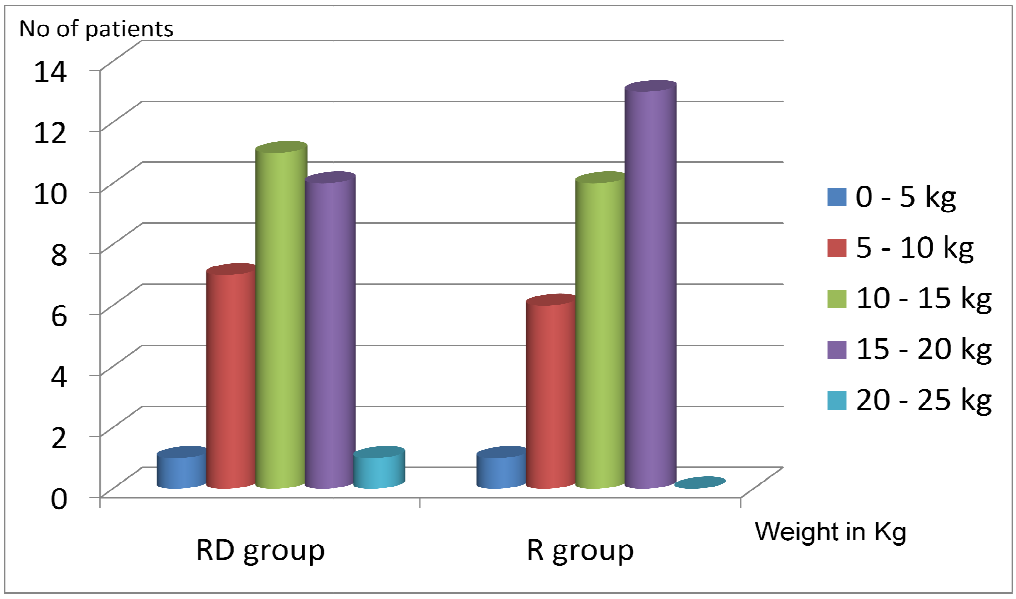
Sex	RD group		R group	
	No	%	No	%
Male	26	86.6	30	100
Female	4	13.7	0	0
Total	30	100	30	100

The above table shows sex wise distribution of RD and R group. In the RD group 86.6% were male and the remaining 13.7% were females. But in the R group, all were males. Both groups were comparable but no statistical difference exists.

Table. 3. Comparison of RD and R groups in respect of their weights

Weight in Kg	RD group		R group	
	No	%	No	%
0 – 5	1	3.3	1	3.3
6 – 10	7	23.4	6	20.0
11 -15	11	36.7	10	33.3
16 – 20	10	33.3	13	43.4
21 – 25	1	3.3	0	0
Total	30	100	30	100
Mean ± SD	12.2 ± 4.2		12.7 ± 3.6	
Significance	P > 0.05			

Figure 2. Comparison of weight distribution in both groups



The mean weight of the RD group was 12.2 ± 4.2 kg and R group was 12.7 ± 3.6 kg. The difference of weight between the two groups was not statistically significant (t = 0.518, d.f = 58 and P > 0.05).

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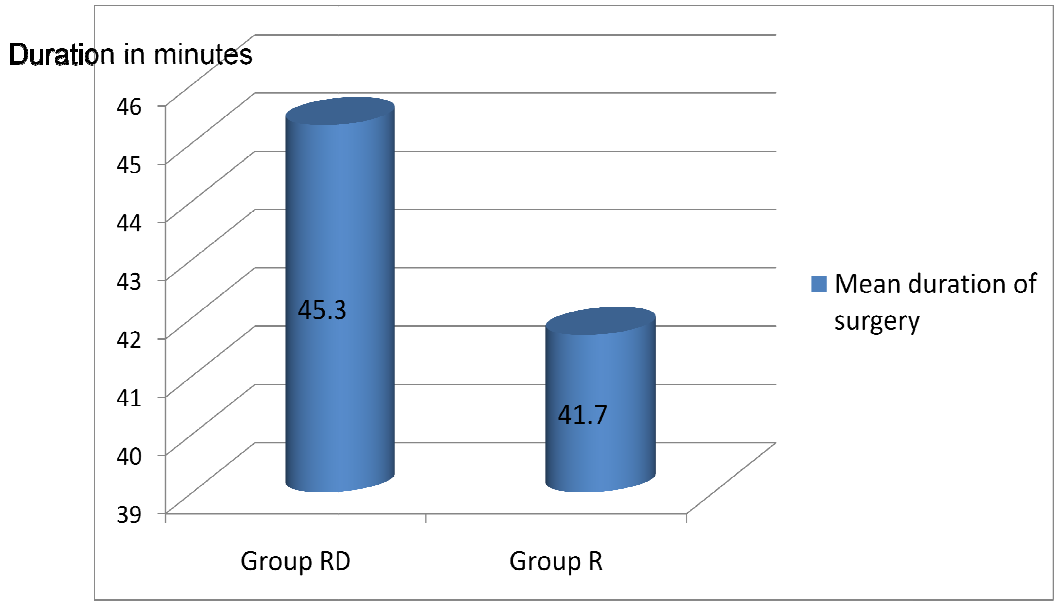
Table .4. Comparison of duration of surgery in both groups

variable	*RD group*		R group		Difference of mean	't'	Significance (p)
	Mean	S.D	Mean	S.D			
Duration of surgery(min)	45.3	17.1	41.7	15.3	3.7	0.874	P > 0.05

Figure 3. Comparison of duration surgery between the two groups

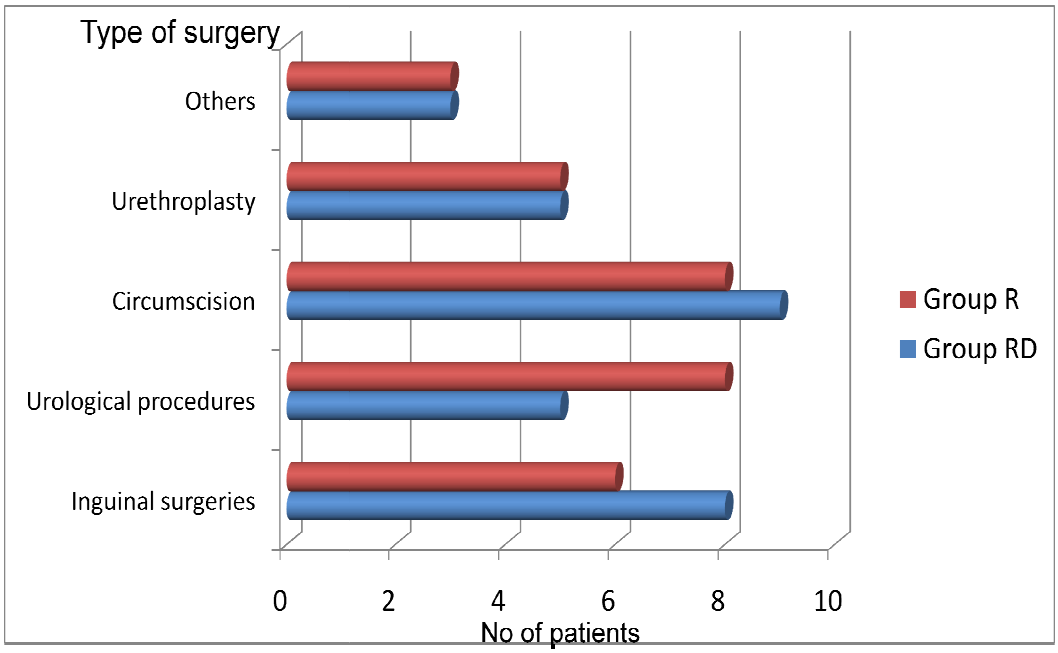


The mean duration of surgery of RD group was 45.3 ± 17.1minutes and R group was 41.7 ± 15.3 minutes. The difference between the means was not statistically significant (P > 0.05).

Table 5. Comparison of type of surgery in both groups

Type of surgery	RD group	R group
Inguinal surgeries	8	6
Urological procedures	5	8
Circumscision	9	8
Urethroplasty	5	5
Others	3	3

Figure.4. Comparison of type of surgery between the groups.

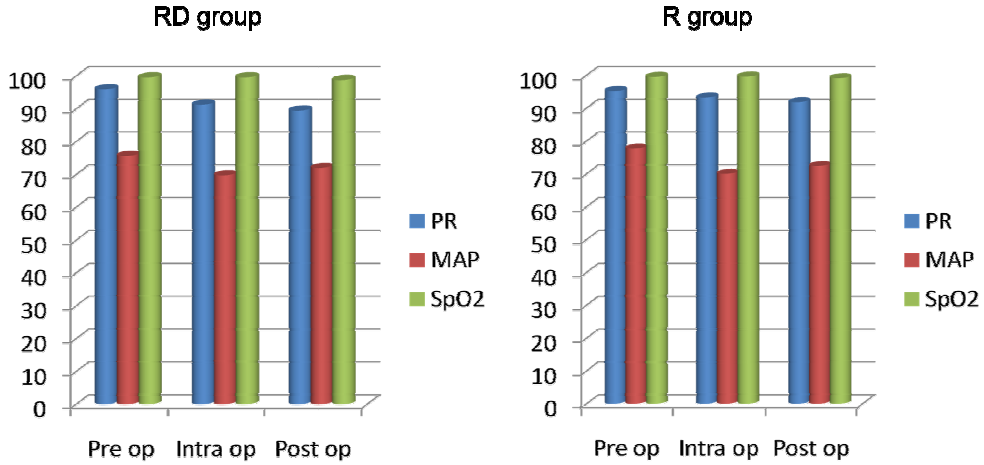


The type of surgeries between the both groups was also comparable but not statistically significant.

Table .6. Comparison of haemodynamic variables

	Variables	RD group		R group		Difference of mean	' t'	Significance (p)
		Mean	S.D	Mean	S.D			
Pre operative	PR	95.9	5.6	95.2	6.9	0.7	0.431	P > 0.05
	MAP	75.6	4.3	77.7	3.9	2.1	1.947	P > 0.05
	SpO2	99.5	0.6	99.5	0.6	0	0	P > 0.05
Intra op	PR	91.2	6.2	93.2	6.6	2.0	1.230	P > 0.05
	MAP	69.7	2.2	70.0	1.3	0.3	0.646	P > 0.05
	SpO2	99.6	0.5	99.6	0.5	0	0	P > 0.05
Post op	PR	89.4	6.7	91.8	6.4	2.4	1.423	P > 0.05
	MAP	71.9	1.9	72.4	1,7	0.5	0.925	P > 0.05
	SpO2	99.1	0.7	99.1	0.7	0.4	0	P > 0.05

Figure.5.Comparison of haemodynamic variables.

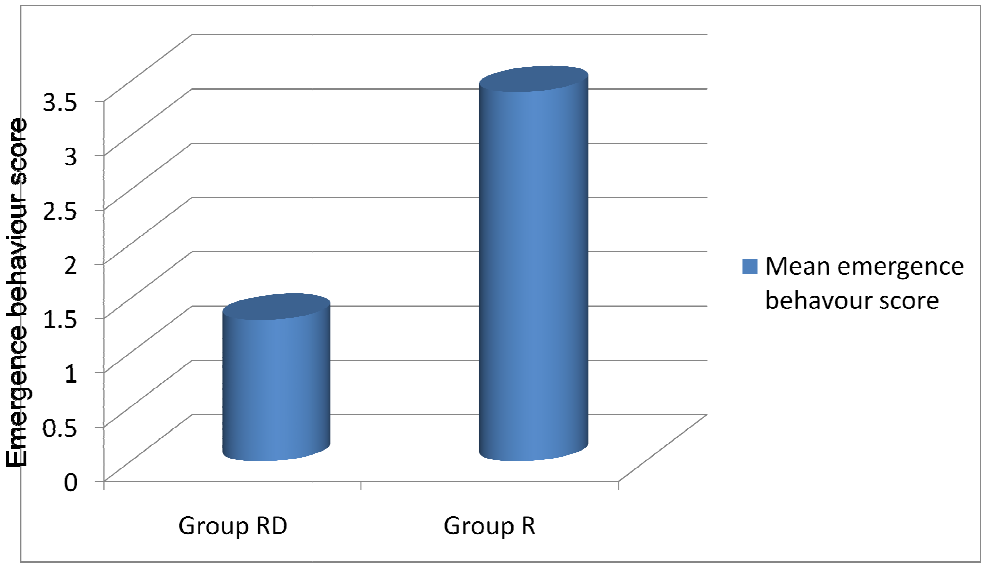


The pre operative, intra operative and post operative haemodynamic changes between the groups were comparable and were not statistically significant (Table 6) and therapeutic interventions were not required.

Table 7. Comparison of Emergence time and Emergence behaviour score.

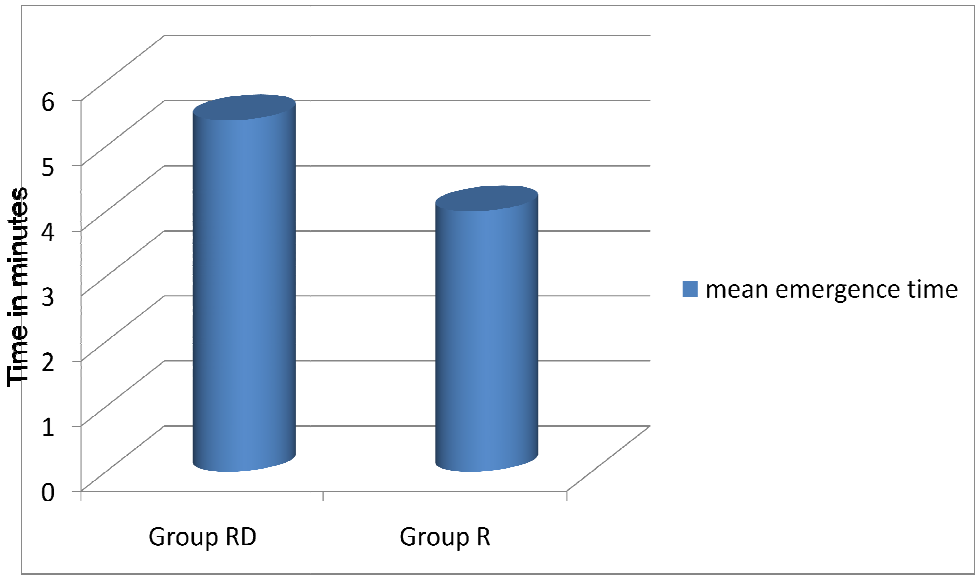
Variables	RD group		R group		Difference of means	' t '	Significance (P)
	Mean	S.D	Mean	S.D			
Emergence time	5.4	1.8	4.0	1.0	1.4	3.798	P < 0.001
Emergence behaviour score	1.3	0.4	3.4	0.5	2.1	17.568	P < 0.001

Figure.6.Comparison of mean emergence behaviour score



The emergence behaviour score of the RD group was 1.3±0.4 and the R group was 3.4±0.5. The difference between the means was statistically highly significant (P < 0.001). This means that R group children were agitated and restless compared to RD group where they were calm and co operative.

Figure.7. Comparison of mean emergence time.



The mean emergence time of RD group was 5.4±1.8 min and the same to the R group was 4.0±1.0 min. The difference of mean between the two groups was statistically very highly significant. (P < 0.001).

Figure.8.Emergence time for all patients

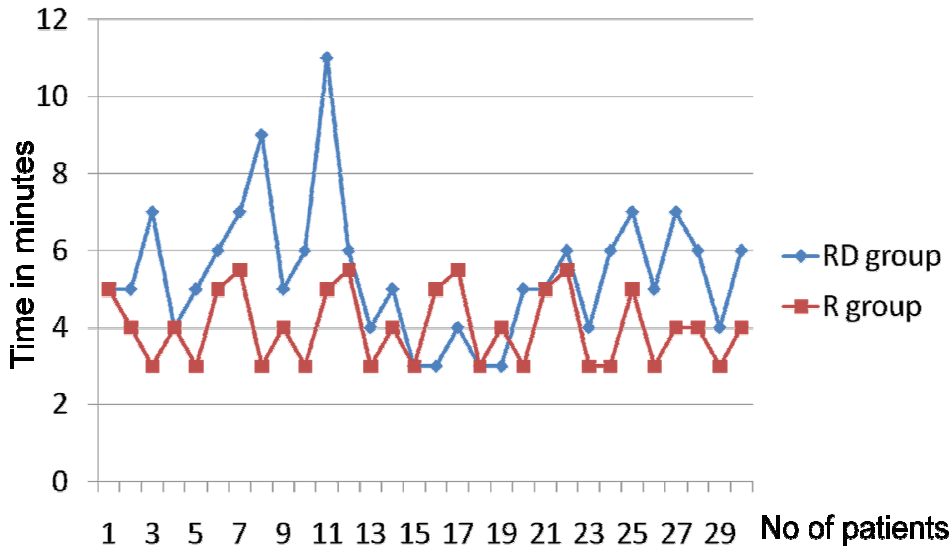
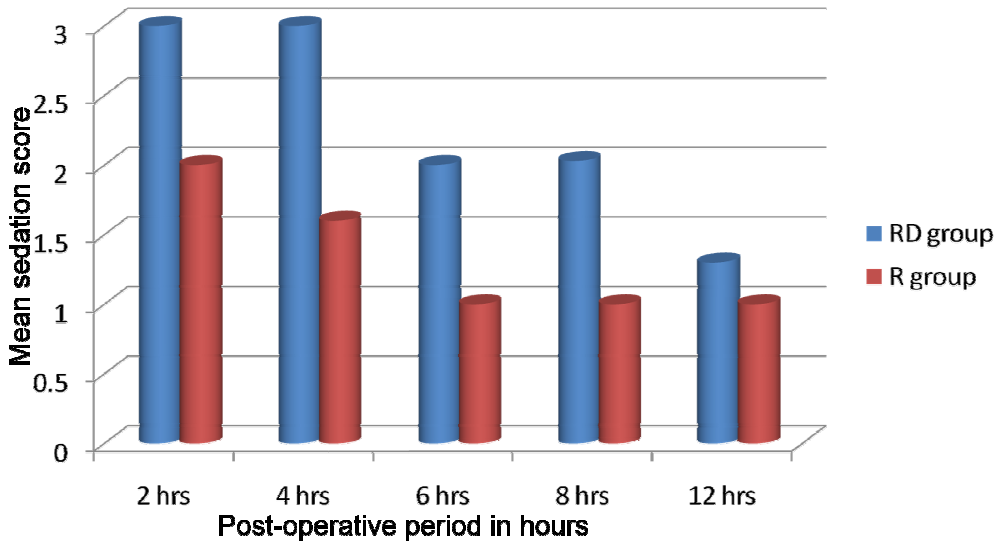


Table. 8. Comparison of mean sedation score in the post operative period.

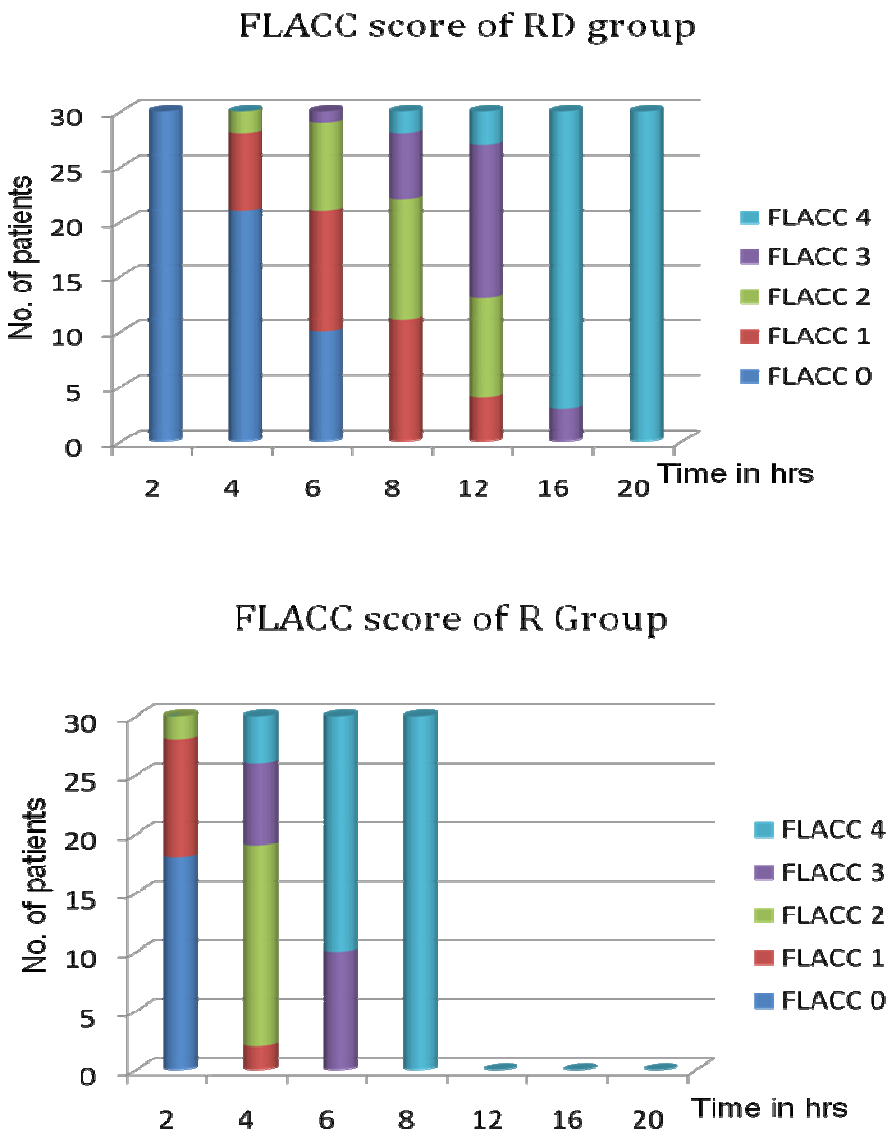
Time in hours	Group RD		Group R		Significance
	Mean	SD	Mean	SD	
2 hrs	3	0.0	2.0	0.0	P < 0.001
4 hrs	3	0.0	1.6	0.5	P < 0.001
6 hrs	3	0.0	1.0	0.0	P < 0.001
8 hrs	2.03	0.2	1.0	0.0	P < 0.001
12 hrs	1.3	0.5	1.0	0.0	P < 0.001

Figure.9. Comparison of sedation score.



The difference of mean sedation score between both groups was statistically very highly significant (P < 0.001). RD group had significant sedation compared to R group that mean RD group children were asleep but easily arousable.

Figure.10.FLACC score of RD and R group children



There was a significant difference between the groups in the FLACC score measured 4th hourly in the post operative period. Group R patients achieved significantly higher FLACC score compared with Group RD, where 20 out of 30 children achieved a FLACC score of 4 at 6th hr compared with 0 patients in Group RD. Whereas, in group RD children had FLACC score 4 at 16th hr of post operative period.

Table 9.Comparison of duration of analgesia

Group	Mean (hr)			Median (hr)			Significance
	Estimate	S.E	CI	Estimate	S.E	CI	
RD	14.4	0.414	13.59 - 15.21	14.5	0.304	13.90 – 15.09	P < 0.001
R	5.5	0.192	5.15 - 5.90	5.5	0.271	4.97 – 6.03	

The duration of postoperative analgesia recorded a median of 5.5hr and 95% confidence interval (CI) (4.97 – 6.03hr) in Group R compared with 14.5hr (13. 90 – 15.09) in Groups RD, with a P-value of < 0.001.

Figure 11. Duration of analgesia of all patients in the study.

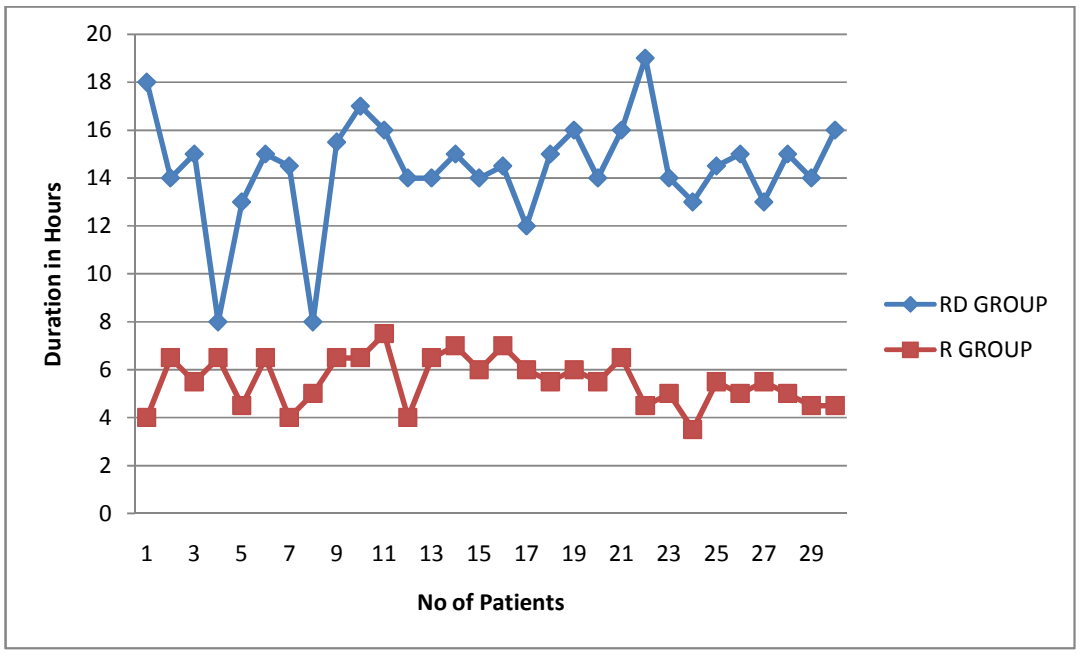
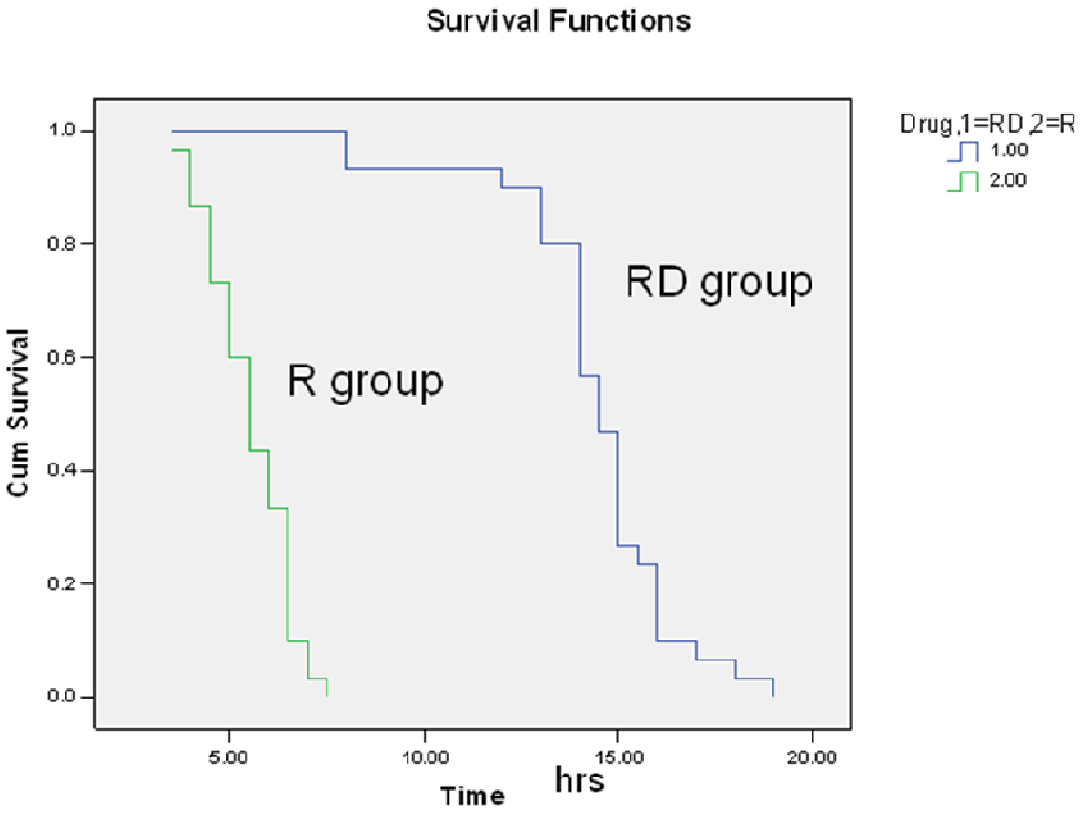


Figure 12. Kaplan- Meier survival curve



This a step line curve showing cumulative survival of all patients in the study for the duration of analgesia in time in hours, with R group showing analgesia time in between 3.5 hrs for the first patient and 7.5 hrs for the last patient who had pain score of 4 in the ascending order. In RD group, it was between 8 hrs and 19 hrs.

Table.10 Postoperative complications

	RD group	R group
PONV	Nil	Nil
Respiratory depression	Nil	Nil
Urinary retention	Nil	Nil
Hypotension	Nil	Nil
Bradycardia	Nil	nil

No episodes of clinically significant postoperative complications such as PONV, respiratory depression, urinary retention, pruritus, hypotension and bradycardia were observed.

DISCUSSION

Motor blockade resulting from caudal block is very distressful to children in the postoperative period and delays hospital discharge. Ropivacaine in comparison to bupivacaine, has a wider margin of safety, less motor blockade, less cardiovascular /neurological toxicity and similar duration of analgesia. It can be safely used for regional anaesthesia and analgesia in the ambulatory setting in paediatrics.[1, 2, 3, 7, 65, 66, 67]

Like clonidine[68,69], dexmedetomidine also enhances the effects of local anaesthetics without increasing the incidence of side effects[70]. A major advantage of dexmedetomidine is its higher selectivity compared with clonidine for α_2A receptors which is responsible for the hypnotic and analgesic effect. Dexmedetomidine, although currently available for i.v. use only, has been successfully administered epidurally for postoperative analgesia in humans in clinical trials.

El-Hennawy et al[4] administered dexmedetomidine and clonidine both in a dose of 2µg/ kg as adjuvant with 0.25% bupivacaine caudally. They found that duration of analgesia was significantly higher in the group receiving bupivacaine-dexmedetomidine mixture [median (95%confidence level): 16 (14-18) hrs] or bupivacaine-clonidine mixture [median (95% confidence level): 12(3-21) hrs] than the group receiving bupivacaine alone [median (95% confidence level): 5 (4-6) hrs]. In our study we found that ropivacaine and dexmedetomidine mixture had a median14.5 hrs (CI 13.90 -15.09) duration of analgesia than ropivacaine alone, which had 5.5hrs(CI 4.97 -6.03)

Neogi M et al[5] compared Clonidine 1µg/kg and Dexmedetomidine 1µg/kg as an adjuncts to Ropivacaine 0.25% for caudal analgesia in paediatric patients and concluded that addition of both clonidine and dexmedetomidine with ropivacaine administered caudally, significantly increases the duration of analgesia. The patients stay haemodynamically stable and there are no undue side effects. The mean duration of analgesia was 6.32±0.46 hours in group R, 13.17±0.68 hours in group C and 15.26±0.86 hours in group D. The prolongation of duration of analgesia was significant in both groups C and D in comparison to group R. The incidence of adverse effects was statistically insignificant between the three groups. In our study we found mean duration of analgesia of 5.5 hrs in Ropivacaine group and 14.4 hrs in dexmedetomidine group.

Saadawy et al[6] compared caudal bupivacaine 0.25% with dexmedetomidine 1µg/kg and caudal bupivacaine alone and showed that the incidence of agitation following sevoflurane anesthesia was significantly lower with dexmedetomidine ($P < 0.05$); The duration of analgesia was significantly longer with dexmedetomidine($P < 0.001$); No statistically significant difference in hemodynamics between both groups; Dexmedetomidine had better quality of sleep and a prolonged duration of sedation($P < 0.05$). This study showed that caudal dexmedetomidine 2µg/kg with 0.25% Ropivacaine also has similar results like Saadawy et al.

Emergence agitation is a frequent side effect of sevoflurane anesthesia in paediatric patients. There is no well defined prophylaxis or treatment, although the incidence of this excitatory behaviour seems to be reduced by the perioperative use of sedative and analgesic drugs. α_2 receptor agonists

may offer advantages in preventing EA because they have both analgesic and sedative properties.

Bock et al.[13] studied the effect of clonidine on EA in 80 children aged 3–8 years undergoing minor day-case surgery who were anesthetized with sevoflurane. The children received a caudal block for perioperative pain relief. A dose of 3μg/kg clonidine was found to prevent agitation whether administered IV or caudally. In the present study using caudal dexmedetomidine 2μ/kg with sevoflurane anaesthesia, the emergence behaviour score was less. This showed that caudally administered dexmedetomidine prevented the emergence agitation following sevoflurane significantly.

SUMMARY

Caudal Dexmedetomidine 2µg/ kg with 0.25%Ropivacaine 1ml/kg for paediatric lower abdominal surgeries achieved significant post operative pain relief up to 15 hours. It has stable hemodynamics in the intra operative and post operative period. It produces less incidence of emergence agitation following sevoflurane anaesthesia and better acceptable sedation in the post operative period. No other analgesic supplementation was needed.

CONCLUSION

This study results conclude that **Caudal Dexmedetomidine** 2µg/kg with Ropivacaine 0.25% effectively prolongs post operative analgesia. It has better quality of sleep and a prolonged duration of arousable sedation. It reduces the emergence agitation following sevoflurane anaesthesia. It produces stable haemodynamics and can be safely used in paediatric day care surgeries.

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A comparative study of caudal Ropivacaine vs Ropivacaine with Dexmedetomidine for paediatric lower abdominal surgeries.

PROFORMA

Name: Age: Sex: wt:

Date: IP No : ASA:

Diagnosis:

Procedure planned:

History :

Investigations:

Hb% urine albumin:

Blood sugar: sugar:

Urea: deposits:

Creatinine:

O/E

Anaemia: activity:

HR: BP:

Pre-med : Inj. Atropine 0.02mg/kg i.m.

Induction : O2 / N2O / Sevoflurane 8%

Airway : LMA

caudal block:

Position : Lt lateral

Needle : 23G i.m. needle

Drug : Group R - 0.25% Ropivacaine 1ml/kg + 0.5ml normal saline

Group RD - 0.25% Ropivacaine 1ml/kg + Dexmedetomidine 2µg/kg in 0.5ml normal saline

Parameters Monitored :

Haemodynamic variables	baseline	Intra op							End of surger
		5min	10min	20min	30min	40min	50min	60min	
HR									
MAP									
SpO_2									
Emergence behaviour score									

Haemodynamic variables	Post op				
	2 hr	4 hr	6 hr	8 hr	12 hr
HR					
MAP					
SpO_2					
Sedation					

FLACC SCORE

TIME	2hr	4hr	8hr	12hr	16	20hr	24hr
FACE 0. No particular smile or expression 1. Occasional grimace or frown, withdrawn, disinterested 2. Frequent to constant quivering chin, clenched jaw							
LEGS 0. Normal position or relaxed 1. Uneasy, restless,tense 2. Kicking or legs drawn up							
ACTIVITY 0. Lying quietly, normal position, moves easily 1. Squirming, shifting back and forth, tense 2. Arched, rigid or jerking							
CRY 0. No cry (awake or asleep) 1. Moans or whimpers ; occasional complaint 2. Crying steadily, screams or sobs, frequent complains							

CONSOLABILITY 0. Content. Relaxed 1. Reassured by occasional touching, hugging or being talked to, distractible 2. Difficult to console or comfort							
TOTAL SCORE							

	Time
Induction	
Caudal block	
Skin incision	
End of surgery	
Emergence	
Analgesic supplementation	

Complications : PONV / urinary retention / pruritus / respiratory depression

RD GROUP

SNO	NAME	AGE/SEX	WEIGHT	*IP no*	TYPE of SURGERY				INTRAOP											
						PRE OP			PR				MAP				SpO2			
						PR	MAP	SpO2	5MIN	10MIN	20MIN	30MIN	5MIN	10MIN	20MIN	30MIN	5MIN	10MIN	20MIN	30MIN
1	arundoss	36/M	10kg	30027	hydrocele	100	81	99	86	88	90	94	70	70	73	73	100	100	99	98
2	mahesh	72/M	20kg	30692	hydrocele	88	83	100	78	80	80	80	75	75	74	74	100	100	99	99
3	mohammed kasim	36/M	14kg	30509	urethroplasty	96	75	100	86	88	90	92	69	69	71	71	99	100	99	100
3	dhanush	10/M	9kg	31230	anoplasty	104	73	100	90	92	94	94	67	67	69	69	99	100	99	100
5	azeem	48/M	15kg	31918	hydroceleand circum	90	76	100	80	82	82	84	70	70	69	69	99	100	100	99
6	mahesh	72/M	15kg	34190	herniotomy	92	83	99	76	78	80	84	72	72	73	73	99	100	100	99
7	VIGNSEH	72/M	18kg	32404	herniotomy	88	73	99	74	75	77	80	67	67	69	69	100	99	100	100
8	jegannathan	48/M	10kg	32260	urethroplasty	96	78	100	84	86	86	88	69	69	69	69	100	99	100	100
9	vasanthan	48/M	12kg	34005	PUV fulguration	104	72	100	84	84	85	86	69	69	73	73	100	100	99	100
10	sathish	60/M	16kg	34243	hernitomy	100	81	100	90	94	94	96	73	73	77	77	100	100	99	100
11	veni	36/F	10kg	20104	soft tissue tumour leg	98	73	99	88	90	90	92	69	69	68	68	99	100	99	100
12	rakesh	30/M	9kg	20667	hydrocele	104	73	99	88	90	94	94	70	70	73	73	99	100	99	100
13	sujith	12/M	8kg	31883	circumscision	110	71	99	90	92	92	94	67	67	67	67	99	100	98	100
14	kaliappan	72/M	18kg	30694	meataldilatation and circu	90	80	99	76	78	78	80	69	69	71	71	100	100	99	100
15	bala	8/M	4kg	29533	circumscision	110	72	99	98	98	99	99	65	65	67	67	100	100	100	100
16	immanuvel	12/M	16kg	35796	circumscision	100	72	98	90	92	94	94	69	69	70	70	100	100	100	99
17	vaishnavi	24/F	10kg	28410	SSG	104	73	99	96	98	98	100	69	69	70	70	100	100	100	99
18	vijaya	11/F	6.5kg	36376	cystoscopy	110	69	99	94	94	96	98	67	67	68	68	99	99	100	99
19	vinoth	12/M	8kg	36398	circumscision	108	75	100	92	94	94	96	69	69	70	70	99	100	99	99
20	dhanush	72/M	18kg	36734	circumscision	90	83	100	76	78	78	84	72	72	73	73	99	100	98	99
21	vikatan	24/M	10kg	37456	urethroplasty	102	73	100	90	92	92	96	70	70	71	71	100	100	99	100
22	vedavalli	72/F	18kg	38467	cystoscopy	90	83	100	84	86	86	88	74	74	75	75	100	99	99	100
23	sukumaran	12/M	10kg	38090	PUV fulguration	108	72	100	90	94	96	98	69	69	70	70	100	100	99	100
24	vishal	36/M	11kg	39616	circumscision	100	74	100	88	90	92	92	70	70	70	70	99	100	99	100
25	bharath	24/M	11kg	38569	urethroplasty	104	73	99	90	92	94	96	69	69	69	69	99	100	99	99
26	esakkimuthu	72/M	17kg	39001	circumscision	88	83	99	75	77	78	80	73	73	74	74	100	100	100	99
27	albert	60/M	16kg	40384	urethroplasty	96	75	100	86	88	90	92	69	69	71	71	100	99	100	99
28	david	18/M	7kg	38998	herniotomy with circum	104	73	100	88	90	94	94	70	70	73	73	100	99	100	99
29	mansiya	24/M	9kg	40527	URS	108	72	100	90	94	96	98	69	69	70	70	100	99	100	100
30	maharajan	36/M	10kg	40705	circumscision	100	74	99	88	90	92	92	70	70	70	70	100	99	100	100

RD GROUP

			DOS	emergence time	emergence behaviour Score	POST OPERETIVE PERIOD (HOURS)																					
EOS						PR					MAP									SpO2							
PR	MAP	SpO2				2	4	6	8	12	2		4		6		8		12		2	4	6	8	12		
86	70	97	40min	5min	1	86	88	90	94	94	90/60	70	96/62	73	98/62	74	100/60	73	100/60	73	99	99	97	99	100		
78	75	98	40min	5min	1	78	80	80	80	80	100/62	75	102/60	74	102/62	75	104/62	76	104/68	80	99	99	98	99	100		
86	69	98	95min	7min	2	86	88	90	92	92	90/58	69	94/60	71	96/60	72	96/62	73	100/60	73	99	98	98	99	100		
90	67	99	40min	4min	1	90	92	94	94	94	90/56	67	92/58	69	92/60	71	92/62	73	92/60	71	99	98	99	99	99		
80	70	100	60min	5min	2	80	82	82	84	84	90/60	70	92/60	69	92/60	71	92/62	73	92/64	73	99	97	100	99	99		
76	72	100	40min	6min	1	76	78	80	84	84	96/60	72	96/62	73	98/62	74	100/62	75	100/62	75	100	100	100	100	98		
74	67	99	35min	7min	1	74	75	77	80	80	90/56	67	90/58	69	92/60	71	94/60	71	94/60	71	99	99	99	99	99		
84	69	98	60min	9min	2	84	86	86	88	90	90/58	69	92/60	69	92/60	71	94/60	71	94/60	71	99	99	98	99	99		
84	69	99	45min	5min	1	84	84	85	86	88	92/60	69	92/62	73	94/60	71	98/60	73	100/60	73	99	100	99	99	99		
90	73	99	40min	6min	2	90	94	94	96	98	100/60	73	104/64	77	104/62	76	102/70	81	104/70	81	99	98	99	99	99		
88	69	99	80min	11MIN	2	88	90	90	92	93	88/56	69	88/58	68	90/58	69	90/58	69	90/60	70	100	99	99	100	99		
88	70	99	45min	6min	1	88	90	94	94	96	90/60	70	94/62	73	98/60	73	98/60	73	98/60	73	100	99	99	100	100		
90	67	97	30min	4min	1	90	92	92	94	96	86/58	67	88/56	67	88/60	69	90/60	70	90/60	70	100	99	97	100	100		
76	69	98	40min	5min	1	76	78	78	80	84	92/60	69	94/60	71	98/62	74	100/60	73	102/60	74	100	99	98	100	100		
98	65	99	30min	3min	1	98	98	99	99	100	88/54	65	88/56	67	90/58	69	90/58	69	92/60	71	100	99	99	100	99		
90	69	99	35min	3min	1	90	92	94	94	96	90/58	69	90/60	70	92/60	71	94/60	71	94/60	71	99	100	99	99	99		
96	69	100	40min	4min	1	96	98	98	100	102	92/58	69	90/60	70	92/60	71	94/60	71	96/60	72	99	100	100	99	98		
94	67	100	35min	3min	1	94	94	96	98	105	86/58	67	88/58	68	88/60	69	90/58	69	90/58	69	99	100	100	99	98		
92	69	100	35min	3min	1	92	94	94	96	98	90/58	69	90/60	70	92/60	71	94/60	71	94/60	71	99	100	100	99	100		
76	72	100	40min	5min	1	76	78	78	84	84	96/60	72	98/60	73	100/60	73	100/62	75	106/60	75	100	99	100	100	100		
90	70	99	45min	5min	1	90	92	92	96	98	90/60	70	92/60	71	94/60	71	94/60	71	94/60	71	99	99	99	99	99		
84	74	98	40min	6min	1	84	86	86	88	88	98/62	74	98/64	75	100/64	75	100/66	77	100/70	80	100	99	98	100	99		
90	69	97	45min	4min	1	90	94	96	98	100	90/58	69	90/60	70	92/60	71	92/60	71	94/60	71	99	98	97	99	99		
88	70	97	30min	6min	1	88	90	92	92	94	94/58	70	94/58	70	96/60	72	98/60	73	98/60	73	99	99	97	99	99		
90	69	98	50min	7min	2	90	92	94	96	98	90/58	69	92/58	69	92/60	71	92/60	71	94/60	71	100	99	98	100	100		
75	73	99	30min	5min	1	75	77	78	80	80	100/60	73	102/60	74	102/62	75	104/60	73	104/60	73	100	99	99	100	100		
86	69	100	95min	7min	2	86	88	90	92	92	90/58	69	94/60	71	96/60	72	96/62	73	100/60	73	99	99	100	99	100		
88	70	100	45min	6min	1	88	90	94	94	96	90/60	70	94/62	73	98/60	73	98/60	73	98/60	73	99	100	100	99	100		
90	69	97	45min	4min	2	90	94	96	98	100	90/58	69	90/60	70	92/60	71	92/60	71	94/60	71	99	100	97	99	99		
88	70	98	30min	6min	1	88	90	92	92	94	94/58	70	94/58	70	96/60	72	98/60	73	98/60	73	98	99	98	98	99		

RD GROUP

POST OPERETIVE PERIOD (HOURS)														Total duration of analgesia hrs
SEDATION					FLACC									
2	4	6	8	12	2	4	6	8	12	16	20	24		
3	3	2	2	2	0	0	0	1	1	3	4			18
3	3	2	2	2	0	1	2	2	3	4				14
3	3	2	2	2	0	0	0	1	3	4				15
3	3	2	2	2	0	1	2	4						8
3	3	2	2	2	0	2	2	3	3	4				13
3	3	2	2	1	0	0	0	1	3	4				15
3	3	2	3	1	0	0	0	1	2	4				14.5
3	3	2	2	1	0	2	3	4						8
3	3	2	2	1	0	0	0	1	1	4				15.5
3	3	2	2	2	0	0	0	1	1	3	4			17
3	3	2	2	2	0	0	1	1	1	4				16
3	3	2	2	1	0	0	0	1	2	4				14
3	3	2	2	1	0	0	0	1	2	4				14
3	3	2	2	1	0	0	0	1	2	4				15
3	3	2	2	1	0	0	1	1	2	4				14
3	3	2	2	1	0	0	1	2	2	4				14.5
3	3	2	2	1	0	1	2	3	4					12
3	3	2	2	1	0	0	1	2	2	4				15
3	3	2	2	1	0	0	1	2	2	4				16
3	3	2	2	2	0	0	1	2	3	4				14
3	3	2	2	2	0	1	2	2	3	4				16
3	3	2	2	1	0	0	1	2	2	3	4			19
3	3	2	2	1	0	1	2	2	3	4				14
3	3	2	2	1	0	0	1	2	3	4				13
3	3	2	2	1	0	0	1	2	3	4				14.5
3	3	2	2	1	0	1	2	3	3	4				15
3	3	2	2	1	0	0	0	2	3	4				13
3	3	2	2	1	0	0	1	3	3	4				15
3	3	2	2	2	0	1	2	3	3	4				14
3	3	2	2	1	0	0	1	3	3	4				16

R GROUP

SNO	NAME	AGE/SEX	WEIGHT	IP no	TYPE OF SURGERY	PREOP			INTRAOP										
						PR	MAP	spo2	PR				MAP				SpO2		
									5MIN	10MIN	20MIN	30MIN	5MIN	10MIN	20MIN	30MIN	5MIN	10MIN	20MIN
1	madan gopal	72/M	15kg	34568	urethroplasty	84	81	99	76	78	79	81	75	76	77	78	98	99	100
2	sethupathy	60/M	15kg	34589	cystoscopy and circm	88	83	100	80	82	83	84	75	76	77	77	99	99	100
3	jeevanathan	12/M	10kg	33584	circumscision	104	72	100	88	90	92	96	68	66	67	69	100	99	100
4	balajothi	72/M	15kg	32934	cystoscopy	94	84	100	90	90	92	94	78	79	79	79	100	99	100
5	karthick	24/M	6kg	32430	circumscision	105	76	100	90	94	96	98	72	72	73	74	99	100	100
6	manthiramoorthy	72/M	15kg	31901	circumscision	88	83	99	80	82	86	88	79	80	81	81	99	100	100
7	ajay	72/M	15kg	31737	PUV fulguration	90	73	99	86	88	90	92	70	68	70	71	100	100	99
8	esakkimuthu	36/M	8kg	31195	hydrocele	90	83	100	90	86	86	88	78	75	74	75	100	100	99
9	tharunraj	72/M	15kg	30644	cystoscopy and biopsy	86	83	100	86	84	87	86	70	68	70	72	100	99	100
10	kavibalan	48/M	15kg	30472	PUV fulguration	100	81	100	100	98	99	96	75	74	77	78	100	99	100
11	madan kumar	7/M	4.2kg	30022	PUV fulguration	92	83	99	94	92	90	92	72	74	75	76	100	99	100
12	pathirakali	60/M	9kg	29377	urethroplasty	82	85	99	90	86	84	80	76	75	78	80	100	99	100
13	ashiq	10/M	8.5kg	35765	circumscision	98	81	99	90	92	90	90	74	76	74	77	100	98	100
14	ganeshamoorthy	60/M	14kg	29736	RA foot- flap cover	98	80	99	102	101	100	101	75	76	78	80	100	99	100
15	thirumalai	72/M	17kg	34831	urethroplasty	98	73	99	98	98	99	99	68	68	69	70	100	100	100
16	nithish kumar	36/M	8kg	36400	herniotomy	100	75	98	100	100	98	99	68	69	68	70	99	100	100
17	thayubala	10/M	8kg	36389	hydrocele	104	73	99	102	100	101	102	66	68	69	70	99	100	100
18	guna	72/M	13kg	34830	cystoscopy	96	77	99	94	92	94	94	67	68	69	70	99	100	99
19	sakthivel	72/M	17kg	36847	circumscision	94	75	100	94	92	92	94	69	70	72	72	99	99	100
20	rahul	48/M	15kg	37510	circumscision	106	73	100	106	104	106	108	69	70	71	72	99	98	100
21	poovarasan	72/M	17kg	37948	herniotomy	94	81	100	90	90	92	94	78	77	79	80	100	99	100
22	ganeshamoorthy	60/M	14kg	29736	RA foot- flap delay	98	80	100	102	101	100	101	75	72	76	77	100	99	99
23	saravanan	42/M	14kg	38598	herniotomy	90	83	100	90	86	86	88	75	76	78	78	100	99	100
24	subash chandrabose	36/M	10kg	39466	orchiopexy	104	72	100	88	90	92	96	65	67	68	69	100	99	100
25	karuppasamy	72/M	15kg	39277	urethroplasty	84	81	99	76	78	79	81	74	76	77	78	99	99	100
26	maria nishanth	36/M	12kg	37853	circumscision	104	72	99	88	90	92	96	66	65	68	69	99	100	100
27	uthandaraman	48/M	13kg	46358	cystoscopy	94	81	100	90	90	92	94	74	75	76	78	99	100	99
28	rajesh kumar	72/M	19kg	40694	herniotomy	94	81	100	90	90	92	94	74	72	77	76	99	100	99
29	abishkumar	36/M	12kg	40690	circumscision	104	72	100	88	90	92	96	65	64	67	68	100	100	99
30	esakkidurai	60/M	12.5kg	40687	rectal polyp excision	94	81	99	90	90	92	94	75	77	78	80	100	100	99

30MIN
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R GROUP

EOS			DOS	Emergence time	emergence behavour score	POST OPERATIVE PERIOD (HOURS)															
						PR					MAP					SpO2					
PR	MAP	SpO2		time	SCORE	2	4	6	8	12	2	4	6	8	12	2	4	6	8	12	
76	78	100	70min	5min	3	76	78	79	81	82	74	77	76	81	81	97	99	99	97	99	
78	78	100	45min	4min	3	80	82	83	84	86	73	75	75	80	82	98	99	99	98	99	
88	70	100	30min	3min	3	88	90	92	96	98	70	71	71	72	73	98	99	98	98	99	
90	80	99	35min	4min	3	90	90	92	94	94	73	73	74	77	79	99	99	98	99	99	
90	76	99	30min	3min	3	90	94	96	98	100	71	72	74	75	76	100	99	97	100	99	
80	82	98	35min	5min	3	80	82	86	88	90	75	79	81	82	83	100	100	100	100	100	
88	72	99	45min	5.5min	4	86	88	90	92	92	73	75	73	76	79	99	99	99	99	99	
88	76	99	35MIN	3min	4	90	86	86	88	90	83	81	82	81	83	98	99	99	98	99	
84	74	99	40MIN	4min	4	86	84	87	86	85	79	81	83	83	83	99	99	100	99	99	
90	80	99	45MIN	3min	4	100	98	99	96	98	75	77	76	81	81	99	99	98	99	99	
92	80	99	45MIN	5min	3	94	92	90	92	93	89	89	86	89	90	99	100	99	99	100	
82	84	100	80MIN	5.5min	3	90	86	84	80	82	85	81	83	85	87	99	100	99	99	100	
90	78	100	35MIN	3min	4	90	92	90	90	92	83	78	76	80	79	97	100	99	97	100	
100	80	100	40MIN	4min	3	102	101	100	101	100	73	73	74	73	74	98	100	99	98	100	
100	70	99	90MIN	3min	4	98	98	99	99	98	73	73	73	73	73	99	100	99	99	100	
100	70	99	35MIN	5min	3	100	100	98	99	99	74	73	73	73	73	99	99	100	99	99	
103	70	98	40MIN	5.5min	4	102	100	101	102	100	73	73	73	73	73	100	99	100	100	99	
96	72	98	40MIN	3min	3	94	92	94	94	92	73	73	73	73	73	100	99	100	100	99	
96	74	100	30MIN	4min	4	94	92	92	94	94	73	73	74	73	74	100	99	100	100	99	
108	72	100	30MIN	3min	3	106	104	106	108	106	72	73	73	73	73	100	100	99	100	100	
95	81	99	35min	5min	4	90	90	92	94	94	73	73	74	77	79	99	99	99	99	99	
102	80	99	40MIN	5.5min	3	102	101	100	101	100	75	73	74	73	74	98	100	99	98	100	
90	80	99	35MIN	3 MIN	4	90	86	86	88	90	85	81	82	81	83	97	99	98	97	99	
98	70	99	30min	3min	3	88	90	92	96	98	70	71	71	72	73	97	99	99	97	99	
83	79	100	70min	5min	4	76	78	79	81	82	74	77	76	81	81	98	100	99	98	100	
98	70	100	30min	3min	3	88	90	92	96	98	70	71	71	72	73	99	100	99	99	100	
96	78	100	35min	4min	4	90	90	92	94	94	73	73	74	77	79	100	99	99	100	99	
96	79	100	35min	4min	3	90	90	92	94	94	73	73	74	77	78	100	99	100	100	99	
95	69	99	30min	3min	4	88	90	92	96	98	70	71	71	72	73	97	99	100	97	99	
95	81	99	35min	4min	3	90	90	92	94	94	73	73	74	77	78	98	98	99	98	98	

R GROUP

POST OPERATIVE PERIOD (HOURS)										Total duration of analgesia hrs
SEDATION					FLACC					
2	4	6	8	12	2	4	6	8	12	
2	2	1	1	1	2	4				4
2	2	1	1	1	0	2	3	4		6.5
2	2	1	1	1	0	2	4			5.5
2	2	1	1	1	1	2	3	4		6.5
2	1	1	1	1	0	2	4			4.5
2	2	1	1	1	0	2	3	4		6.5
2	1	1	1	1	1	4				4
2	2	1	1	1	0	2	4			5
2	1	1	1	1	0	2	3	4		6.5
2	2	1	1	1	0	2	3	4		6.5
2	1	1	1	1	0	1	3	4		7.5
2	2	1	1	1	2	4				4
2	1	1	1	1	0	3	3	4		6.5
2	2	1	1	1	1	2	3	4		7
2	1	1	1	1	1	3	4			6
2	2	1	1	1	0	2	3	4		7
2	1	1	1	1	0	2	4			6
2	2	1	1	1	0	2	4			5.5
2	1	1	1	1	0	3	4			6
2	2	1	1	1	1	2	4			5.5
2	1	1	1	1	0	2	3	4		6.5
2	2	1	1	1	1	3	4			4.5
2	1	1	1	1	0	2	4			5
2	2	1	1	1	1	4				3.5
2	2	1	1	1	1	2	4			5.5
2	2	1	1	1	0	3	4			5
2	1	1	1	1	0	1	4			5.5
2	2	1	1	1	1	2	4			5
2	1	1	1	1	0	3	4			4.5
2	2	1	1	1	1	3	4			4.5